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THE PROJECTION OF THE VESTIBULAR SYSTEM ON THE CENTRAL NERVOUS SYSTEM
A PET STUDY

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Introduction

The internal representation of space involves the integration of different sensory inputs (visual, somatosensory/proprioceptive, vestibular) yielding reference frames which are not based on individual peripheral sensory codes, being organized instead in ego-centred and object- or environment-centred coordinates (Ventre 1984, Vallar 1993, Graziano 1994, Karnath 1994, Andersen 1997). The harmonic equilibrium between the elements of the system results in developing awareness of space, and the stability of body posture and movement. The network involves a dynamic co-operation between the cortical and subcortical structures, as well as a permanent change in the activated and deactivated elements. If antagonistic sensory modalities get into the system or the centre operates pathologically, a disturbance in spatial orientation of the body develops, which the patient experiences as vertigo.

Vertigo, dizziness, and disequilibrium are common complaints of patients of all ages, particularly the elderly. As presenting symptoms, they occur in 5-10% of all patients seen by general practitioners and 10-20% of all patients seen by neurologists and otolaryngologists (Brandt 2000). In ENT practice it is treated as vestibular vertigo, the characteristics of which (determined direction, feeling of rotatory vertigo, vegetative signs) are clearly distinguished from dizziness of non-vestibular origin.

In the background of vestibular vertigo there is an imbalance between the both-sided end-organ. Recovery can occur in two different ways, either by curing the end-organ or by developing central compensation. Central compensation originates from the plasticity of the central nervous system, which manifests in the accommodation to the modified peripheral sensorial status.

It is important to understand the compensation process in the central nervous system in order to make a prognosis and decide on a treatment protocol for the disease (vestibular training, effect of medicines, etc). Where do the cerebral changes caused by the vestibular end-organ in healthy and pathologic individuals appear? Which areas participate in the vestibular compensation procedure? What kind of methods can be used to study this issue?

Intensive research has been done into the vestibular system in our country. Róbert Bárány was awarded the Noble prize for his research into the physiology and patophysiology of the equilibrium system in 1914. With his observations of outstanding merit, János Szentágothai also contributed to our understanding of the fine structure of the vestibular system (Szentágothai 1950).

The periphery of the vestibular system and its relationship with the central nervous system up to the level of the brainstem is well defined. We have fewer data on subcortical nuclei though, and the cortical representation has long been in the centre of research.

Although animal studies have been providing plenty of information, real outlook for human research has just opened up. In the past information was mainly provided by intraoperative electrophysiological measurements and through observation of brain lesions, but recent development has introduced brain activation tests which are performed by single-photon emission tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI). They measure regional cerebral blood flow (rCBF). The physiological basis of these measurements is that the changes in neuronal activity are in close connection with rCBF (Ganong 1999). Nowadays it is widely accepted that an increase in blood flow indicates an increased function (activation), while its decrease refers to a reduced function (deactivation) (Wenzel 1996, Brandt 1998, 2000, Bense 2001, Bottini 2001).

Bottini and co-workers were the first to describe in detail activated brain areas after caloric vestibular stimulation in 1994 (Bottini 1994). It was surprising to find the activated

areas exclusively on the other side of (contralateral to) the stimulation. This presumes a strictly one-sided crossed pathway. Later a slightly modified trial proved both-sided (ipsi- and cotralateral) activation with contralateral dominance (Bottini 2001). It corresponds to other researchers' (Bucher 1998, Lobel 1999, Brandt 2000, Kisely 2000, 2001, Bense 2001) data.

In contrast, Takeda and co-workers described the cortical perception of vestibular stimulation in the parieto-temporal lobule of the non-dominant hemisphere (Takeda 1995).

PET and fMRI studies have shown that not only does caloric or galvanic stimulation activate the vestibular cortex, but it also deactivates the both-sided occipital visual cortex. The reverse is also true, i.e. the visual stimulus activates the visual cortex, while it deactivates the vestibular area. This observation correlates to the hypothesis which supports the existence of a reciprocal visual-vestibular interaction for the perception of spatial orientation and movement (Wenzel 1996, Brandt, 1998, 2000). Further investigations have also proved a nociceptive-somatosensory interaction. (Bense 2001).

The physiological importance of the phenomenon is that the suppression of an inadequate stimulus should not cause any disturbance in central processing, and that adequate shifting toward the other sign should help accurate central organisation (Wenzel 1996, Brandt 1998, 2000, 2002, Bense 2001).

There are several peripheral simulation methods applied to vestibular research (optokinetic, galvanic, caloric, neck vibration tests), each of which also contains stimuli of non-vestibular origin (Bottini 1994, 1995, Brandt 1998, Bucher 1998, Bense 2000). There is no method without extravestibular modalities (Bense 2001). In previous studies, attempts have been made to eliminate the influence of tactile, nociceotive and auditory effects on the results of measurements. (Bottini 1994, 2001, Wenzel 1996, Brandt 1998, Bense 2000).

The following questions arise as to whether the methods applied to the elimination of non-vestibular components are adequate, and whether or not extravestibular effects disturbing the measurements will develop in response to a vestibular stimulus.

Objectives

1. To map the projection of the vestibular system on the central nervous system, using rCBF measurements. We also considered the increase and decrease in brain activity. We wondered if there were further cortico-cortical connections besides the ones described before. The experiments were performed on healthy volunteers.

2. To localise extravestibular components. Both the results in the literature and our own experience have shown that a vestibular stimulus affects not only the vestibular system but other sensorial and motor regions too. Consequently, apart from the vestibular effects required in a given experiment, visual, tactile, acustic and nociceptive, i.e. extravestibular responses are also elicited. In this research we studied patients suffering from one-sided total chronic vestibular lesion. Similarly to the healthy group, we evaluated both the activation and deactivation in these patients. Analysing their data, the question arose as to whether or not there were further cortico-cortical connections.

3. After eliminating extravestibular effects, we aimed to define the regions activated by a purely vestibular stimulation. In this way we wanted to point out a "core region" that has the most intensive relationship with the vestibular system, which is responsible for the body's spatial orientation. We studied how this region

compared to the regions other researchers had found as a result of their experiments carried out for a similar purpose.

4. A physiological response, similar to the symptoms of one-sided acute vestibular lesion, can be triggered off by cold caloric stimulation. In both cases a nystagmus directed to the opposite side with vestibulo-spinal signs directed to the same side will develop. Consequently, a harmonic vestibular syndrome can be observed. The following questions arise: Behind the similar peripheral signs, are the changes in cortical activity also similar? Can cold caloric stimulation be used as a model for acute vestibular lesion? Are there preliminary signs of the development of central compensation, and what are they?

Patients and methods

Our research was conducted on three groups of people.

1) A group of healthy people.
2) A group of patients with chronic vestibular lesion who have undergone surgery on the of cerebello-pontine angle tumour.
3) A group of patients with acute vestibular lesion (neuronitis vesatibularis).

In the first and in the second group PET perfusion tests were performed with both-sided caloric stimulation and without stimulation - at rest. In the group of acute vestibular lesion, measurements were performed only at rest. We gave nine test to each person in the first and in the second group, and three in the third group, so we performed 117 tests altogether.

Caloric stimulation

The caloric test was performed using 30 ml iced water (0^{o}C) irrigation to the external ear canal for 60 s (Bottini 1994, 2001, Kisely, 2000, 2001, 2002 a, b, Emri 2003).

PET image analysis

Each subject underwent magnetic resonance scanning of the head before PET examination; this was performed by a 1.5 T Siemens Magnetom SP63 scanner using *T*1-weighted three-dimensional gradient echo acquisition (*TR*=13 ms, *TE*=5 ms, flip angle=10°). Images were sampled as 2.5 mm contiguous transverse slices with a matrix size of 192×256.

The PET studies were performed using a GE 4096 whole-body PET scanner, producing 15 slices, 6.5 mm thick, and with a transaxial resolution of 5-6 mm. Special attention was paid to the circumstances of the PET measurements, as we wanted to exclude all the stimuli that could be excluded. Therefore, the subjects were placed in a comfortable position on their backs for the duration of the experiment, and their head motion was reduced with the use of a comfortable, soft (covered, moulded polyurethane foam) head fixation system. The authors asked the subjects to relax completely, but their alertness was checked upon regularly between stimuli. The lowest scan plane was aligned to the orbitomeatal line. A transmission scan lasting for 15 min was performed using a ^{68}Ge pin source. The start of stimulation coincided with an intravenous injection of ~45 mCi ^{15}O-butanol and lasted for 3 min. Data acquisition was initiated at the onset of the injection of the tracer and consisted of 36 frames (36×5 s).

After the necessary corrections (random coincidence, dispersion, tissue weakening), the scans were reconstructed with a 4.2 mm Hanning filter; the images of the dynamic examination were then integrated over 90 s after the time of the arrival of the tracer in the brain. These perfusional tracer accumulation images were later used in both the image registration and spatial normalization procedure and in the statistical analysis.

On examination of each subject, a native, *T*1-weighted, three-dimensional SPGR axial magnetic resonance image was made (Siemens Magnetom SP63 1.5 T; *TR*=12.5 ms, *TE*=5 ms). The magnetic resonance images were transformed into the Talairach system of coordinates (10, 20) by the MNI Automated Non-Linear Registration package. From the spatially normalized magnetic resonance images, the scalp, skull and meninges were eliminated by a standard brain mask. These masked magnetic resonance images were transformed back into the subjects' native space and were used for MRI-PET registration performed by the Automated Image Registration (AIR) program package. The automated MRI-PET registration was controlled and, in some cases, corrected by an interactive image registration and fusion program. The registered PET images were transformed into the Talairach space by the transformation determined using the appropriate magnetic resonance image. To adjust for differences in the subjects' individual neuroanatomy, an isotropic gaussian smoothing filter was applied [full width at half-maximum (FWHM)=16 mm].

The spatially normalized and filtered PET data were subjected to statistical parametric mapping analysis by the method of Friston *et al*. using the SPM99 software package. With the help of Friston's analysis of covariance (ANCOVA) model, the differences in the global perfusion of the individual examinations were eliminated; then, a subtractional statistical image was compiled in such a way that the images belonging to the brain areas that were considered to be significantly activated were selected on the basis of the *P*<"<0.001 probability scale. The images were normalized for global blood flow differences with ANCOVA, and the statistical significance of perfusion changes was tested using the general linear model: multisubject analysis with subject interaction with three conditions and three replications. Between-task comparisons were performed on a voxel-by-voxel basis with *P*<"<0.001 (*T*">4.28, *f*=28) uncorrected threshold; the cluster size threshold (minimal number of 8 mm^3 voxels) was 100.

The locations of increasing and decreasing rCBF during caloric vestibular stimulation (CVS) related to the reference study were delineated from the SPM{*T*} map by high threshold *T*">4.38 and by cluster size">100 voxels. These activated and deactivated areas were overlaid on the averaged *T*1-weighted image of the population.

Results and discussion

Observations on healthy volunteers

After the experiment we found several activated and deactivated brain areas in the group of healthy volunteers.

Of the previous authors it is Brandt et al. who reported on an increased brain activity in the Br.6. area, using a PET study with warm stimulation (Brandt 1999, 2000 a). The area is a part of the frontal eye field (Paus 1996). Its activity is presumably in connection with the eye movement caused by the vestibular stimulus. We also assume that the increased activity is connected to the strengthening of skeletal muscles, which develops during the test. Consequently, the effect exerted on skeletal muscles by the vestibular system may have a cortical representation. (Kisely 2000 a, b, 2001).

In their report in 1994, except for one region Bottini et al. described an increased activity in exclusively contralateral areas (Bottini 1994), which agrees with Tuohimaa's observations. In the current study we observed both-sided increase in activity, although the ipsilateral change was localised in a smaller area (Kisely 2000 a, b, 2001).

Studying the deactivated regions, we found a rich network of areas. Similarly to Paulesu, we also found mainly an ipsilateral decrease (Paulesu 1997). Previous authors had described the reciprocal operation of visual and vestibular areas. On the basis of previous

study results, the deactivation of visual and visual associative cortex (Br.17, 18, 19, 39) could be expected. Data on the temporal cortex – Br. 20, 21, 38 (Paulesu 1997) - had also been published before. A part of these regions is well-known as the limbic associative cortex, the central part of which plays an important role in declarative memory.

We observed a significant decrease in activity in two areas of the frontal lobule (Br. 8, 11). As far as the function is concerned, the deactivation of Br 8 area is reasonable, since it is part of the frontal voluntary gaze centre.

Vitte et al. were the first to point out in humans the functional relationship between the hippocampus and vestibular system, which was observed as a simultaneous increase in activity. The question arises as to why we found a decrease in blood flow in our current study. We attribute the difference to the difference in study protocol. Vitte et al. applied a less intensive stimulus (12 C^o water temperature) and tried to inhibit a nystagmus response by instructing the patient to fix their eyes during the measurements. The differences in the results can probably be explained by this.

Study results of patients suffering from chronic vestibular lesion

Among the stimulation methods of the peripheral vestibular system (optokinetic, galvanic, caloric and neck vibration tests) we can also find stimuli of non-vestibular origin. In previous studies, attempts have been made to eliminate the influence of tactile, nociceptive and auditory effects on the results of measurements during caloric stimulation.

The question arises as to what other non-vestibular elements can the changes caused by caloric stimulation add to the pattern of rCBF changes in the central nervous system.

In order to answer this question, we would need a model that makes it possible to study the changes in rCBF, caused by an extravestibular stimulus during total vestibular

deprivation. Patients operated on for cerebello-pontine angle tumour are suitable for our purposes.

Our results provide new information on the complex nature of a caloric stimulus by exposing its components and revealing their effect on the central nervous system.

The elimination of non-vestibular originating effects is simplest during the caloric test. Because the duration of the reaction after stimulation is long, the time window of data collection can be moved, that is, it is possible to wait until after the stimulation. It is obvious that the sooner data collection begins, the stronger the reaction will be. At the same time, the possibility of the participation of extravestibular effects within the reaction increases. If we increase the waiting time, we reverse this relationship. During our measurements the investigated healthy subjects reported unpleasant pain and feeling of cold. On the basis of this experience, the authors decided to investigate whether there was a significant cortical response when the vestibulo-ocular reflex was excluded. If there was a significant reaction, the brain territories in which activation and deactivation occurred were determined.

After operation to remove a cerebello-pontine angle tumour, the role of vestibular or acoustic effects can be excluded. Only tactile, heat and pain effects are observed.

Changes in rCBF caused by extravestibular stimuli

The anterior portion of the cingulate gyrus (Br. 32) is a well-known part of the cortical region activated by a pain stimulus. In the case of pain caused by cold and warm stimuli, and after galvanic stimulation that did not contain a vestibular component, an increase in rCBF was observed. This increase, however, was not verified after laser stimulation. The medial frontal gyrus and the insula (partially or completely), the inferior parietal lobula and the post-central regions (SI, SII) all take part in the creation of the territories activated by pain, heat and tactile stimuli. The size or absence of these territories can be explained by the place,

power and type of stimuli. On comparison of the above areas with the areas showing an increase in rCBF on caloric stimulation in the healthy control group, similarities can be found. These include the posterior insula, post-central gyrus, inferior parietal lobe, area SII and temporoparietal junction. This gives rise to the possibility that these areas, partially or fully, are in connection with the extravestibular stimulus.

During the application of the caloric stimulation method, however, a non-vestibular originating cortical reaction is also created, which can be connected to the subjective feeling of heat and pain. As a result of this, regions are activated which are not in connection with the spatial orientation of the body.

Previously, several authors have revealed the deactivation of the visual cortex during caloric stimulation.

The decrease in rCBF caused by a galvanic cutaneous pain stimulus has been verified. The medial temporal gyrus (Br. 19, 39), the occipital gyrus (Br. 19, 18), the lips of the central sulcus (Br. 4, 3) and the post-central gyrus (Br. 3, 2) were deactivated when stimulated. In analogy with the inhibitory vestibularvisual interaction, the existence of an inhibitory nociceptivesomatosensory interaction is emphasized. This mechanism works if the galvanic test is used for both vestibular and isolated pain stimulus. The role of the deactivation of the visual cortex has not been discussed.

The reciprocal vestibularvisual inhibitory interaction is a well-defined physiological function. It describes the simultaneous activation of the visual cortex with the decrease in rCBF in the vestibular region. The reaction caused by the two sensory modalities shifts towards one or the other on the basis of the dominance of the stimulation.

During our experiment, the deactivation of the visual cortex was observed. Because the role of the vestibular stimulus is excluded, we have to presume an inhibitory extravestibular effect on V2V5. In our opinion, there must be a nociceptivevisual interaction

as well, in analogy with the vestibularvisual and nociceptivesomatosensory inhibitory interactions.

Comparative analysis of the group of healthy individuals and the group of patients with chronic vestibular lesion

Our results have proved that the retroinsular and SII cortex is the human analogue for PIVC. This area is part of the multimodal network of the central nervous system, related to the spatial orientation of the body. This has been supported by electrophysiological, histological and functional imaging techniques. The perfusion changes caused by vestibular stimulation are the most pronounced in this area, consequently it can be considered a "core region", a dominant vestibular area (Guldin 1998, Brandt 1999, 2002).

The multisensory areas, showing an increase in activity in our previous studies, are also parts of the cortical network, which is responsible for integrating spatial orientation. When at work, however, their function related to the vestibular stimulus is less dominant compared to the "core region" which we have verified.

Results of patients suffering from acute vestibular lesion

In our study we sought for the similarity of cortical projection between cold caloric stimulation and one-sided vestibular lesion. We concluded that CNS response to caloric stimulation and the change in the brain activity of patients with neuronitis vestibularis would only partially affect the same hemispherical areas. While the former is a cortical representation of a hyperacute disturbance of equilibrium, the latter indicates a change in rCBF, where the dynamic balance of stimulatory and inhibitory procedures may change and which is caused by a process in progress, affecting patients in various stages of the disease but

showing good recovery prospects. We attribute the difference between the two areas to spontaneous compensatory procedures in the pathological state.

Our results can be interpreted as follows:

1. By presenting a deactivated area, we were the first to verify the involvement of the hippocampus in the operation of a healthy vestibular system.
2. We were the first to publish the existence of nociceptive-visual inhibition.
3. We produced a model in which the vestibular and extravestibular elements can be distinguished.
4. We pointed out that cold caloric stimulation also contains extravestibular elements.
5. We verified the location of a "core region" which has the most intensive relationship with the vestibular stimulus.
6. According to our preliminary studies, cold vestibular stimulation may not serve as a model for acute vestibular lesion, as it could be assumed on the basis of a physiological response.

The thesis is based ont he following publications:

1. Emri M., Kisely M., Lengyel Zs., Balkay L., Márián T., Mikó L., Berényi E., Sziklai I., Trón L., Tóth Á.: Cortical projection of peripheral vestibular signaling, J. Neurophysiol., 2003, (in press)
   IF: 3.15

2. Emri M., Bogner P., Balkay L., Tóth Á., Kisely M., Weisz J., Ádám Gy, Glaub T., Berecz R., Repa I.: [^{15}O]-butanol PET-vizsgálatok térbeli standardizálása szegmentált, T1-súlyozott MRI-felvételek segítségével. Orv. Hetil., 2002, 142, 21, Suppl. 3, 1249-1251.

3. Kisely M., Tóth Á., Emri M., Lemgyel Zs., Kálvin B., Horváth G., Trón L:, Bogner B., Sziklai I.: A vestibularis ingerület központi idegrendszeri feldolgozásának agyaktivációs vizsgálata pozitronemissziós tomográfiával. Orv. Hetil., 2000, 141, 2807-2813.

4. Kisely M., Tóth Á., Emri M., Lengyel Zs., Horváth G., Sziklai I., Trón L.: The effect of vestibular stimulation on the regional cerebral blood flow: Positron emission tomography study, 4th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery, Berlin (Germany), May 13-18, 2000, Suppl., Editors: K. Jahnke, M Fischer, Monduzzi Editore, 2000 b, 42-53.

5. Kisely, M., Tóth, Á., Emri, M., Lengyel, ZS., Kálvin, B., Horváth, G., Trón, L., Bogner, B., Sziklai, I.: Verarbeitung vestibulärer Impulse im Zentralnerversystem. HNO., 2001, 49, (5), 347-354.
IF: 0.62

6. Kisely M., Emri M., Lengyel Zs., Kálvin B., Horváth G., Trón L., Mikó L., Sziklai I., Tóth Á.: Changes in brain activation caused by caloric stimulation in the case of cochleovestibular denervation – PET study. Nucl. Med. Comm., 2002 a, 23, 967-973.
IF: 1.19

7. Kisely M., Tóth Á., Emri M., Lengyel Zs., Kálvin B., Horváth G., Bogner P., Szilkai I., Trón L.: Patológiás és indukált perifériás vestibularis egyensúlyzavar központi idegrendszeri hatása. Orv. Hetil., 2002 b, 143, 21, Suppl.3, 1330-1332.

8. Tóth Á., Lampé I., Kisely M.: A neuronitis vestibularis etiológiájáról
Fül-orr-gégegyógy. 1991 a, 37, 19-23.

9. Tóth Á., Kisely M., Lampé I.: A forgatásos reakciók paramétereinek változása neuronitis vestibularisban. Fül-orr-gégegyógy. 1991 b, 37, 213-217.

10. Tóth Á., Kisely M., Lampé I.: Vestibular neuronitis reflected in rotatory test
The new frontiers of Oto-Rhino-Laryngology in Europe, Monduzzi Editore
Bologna, 1992, vol. I. 391-393.

11. Tóth Á, Kisely M., Lampé I., Mahunka I: Neurontis vestibularis eigentümlichkeiten der thermischen Reaktionen,. Oto-Rhino-Laryngologica-Nova, 1993, 3, 263-266.

12. Tóth, Á., Kisely, M., Répássy, G.: A proposal for introducing a modified vestibular index in neurology. Eur.Arch. Otorhinolaryngol., 1996, 253, 381-384.
IF: 0.459

LIST OF PUBLICATIONS:

1. Csarkó P., Lampé I., Kisely M., Anwar F.: Fül-orr-gégészeti malignus tumorok halmozott családi előfordulásának esetei
Fül-orr-gégegyógy. 33, 142-144 (1987)

2. Tóth Á, Kincses Gy., Jókay I., Lázár J., Késmárki K., Kisely M., Farkas T.: Citosztatikus terápiával szerzett tapasztalataink
Fül-orr-gégegyógy. 34, 201-206 (1988)

3. Szűcs J., Mikó T., Kisely M., Lampé I.: A Melkersson-Rosenthal-Syndroma egy esete klinikánkon
Fül-orr-gégegyógy. 35, 108-110 (1989)

4. Tóth Á., Lampé I., Kisely M.: A neuronitis vestibularis etiológiájáról
Fül-orr-gégegyógy. 37, 19-23 (1991)

5. Kisely M., Gombi R., Tóth Á., Lampé I.: Rövid alternáló nystagmusrohamokat okozó kisagy-hídszögleti congenitalis cholesteatoma
Fül-orr-gégegyógy. 37, 57-59 (1991)

6. Tóth Á., Kisely M., Lampé I.: A verticalis nystagmusról két esetünk kapcsán
Fül-orr-gégegyógy. 37, 81-84 (1991)

7. Tóth Á., Kisely M., Lampé I.: A forgatásos reakciók paramétereinek változása neuronitis vestibularisban
Fül-orr-gégegyógy. 37, 213-217 (1991)

8. Á.Tóth., M. Kisely, I. Lampé: Spontan heilender vertikaler Nystagmus
Otorhinolaringol Nova 1, 260-262 (1991)

9. Lampé I., Kisely M., Pap U.: A tűaspiráció szerepe a peritonsillaris tályog diagnosztikájában és terápiájában
Fül-orr-gégegyógy. 38, 54-57 (1992)

10. Á. Tóth, I. Lampé, M. Kisely, R. Gombi: Periodisch alternierender Nystagmus und kongenitalis cholesteatom
Oto-Rhino-Laryngologica-Nova, 2, 91-93 (1992)

11. Á. Tóth, M. Kisely, I. Lampé: Vestibular neuronitis reflected in rotatory test
The new frontiers of Oto-Rhino-Laryngology in Europe, Monduzzi Editore Bologna, vol. I. 391-393 (1992)

12. I. Lampé, T. L. Rácz, L. Tóth, M. Kisely: Otoacustic emissions in normal and hearing impaired children
The new frontiers of Oto-Rhino-Laryngology in Europe
Monduzzi Editore, Bologna, Vol. I., 457-459 (1992)

13. Tóth Ágnes dr., Kisely Mihály dr., Lampé István dr., Mahunka Imréné dr.: Gyorsan gyógyuló betegség-e a neuronitis vestibularis? (A termikus reakciók sajátosságai)
Fül-orr-gégegyógy. 39, 47-53 (1993)

14. Kisely Mihály dr., Tóth Ágnes dr., Lampé István dr.: A vízzel és levegővel történő caloricus ingerlés összehasonlítása
Fül-orr-gégegyógy. 39, 54-58 (1993)

15. Á. Tóth, M. Kisely, I. Lampé, I. Mahunka: Neurontis vestibularis eigentümlichkeiten der thermischen Reaktionen
Oto-Rhino-Laryngologica-Nova, 3, 263-266 (1993)

16. Tóth Ágnes dr., Kisely Mihály dr., Répássy Gábor dr.: Javaslat a módosított vestibularis index bevezetésére az otoneurológiában. A neuronitis vestibularis osztályozása.
Fül-orr-gégegyógy. 41, 29-34 (1995)

17. Tóth Á., Benkő K., György I., Kisely M., Lampé I.: Szédüléses tünetekkel járó tágult aqueductus vestibularis syndroma
Fül-orr-gégegyógy. 41, 206-210 (1995)

18. Tóth Á., Kisely M., Répássy G.: A proposal for introducing a modified vestibular index in neurology
Eur Arch Otorhinolaryngol 253, 381-384 (1996)
IF: 0,459

19. Tóth Á., Kisely M.: Vertigos betegek kezelése Betaserc-kel
MOTESZ-Solvay Pharma tudományos pályázat II. díj. 1995. dec. 15.

20. Kisely M., Tóth Á., Répássy G.: The possibility of investigation of vestibulospinalsystem with CCG in children-normal values
3rdEuropean Congress of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS)
Budapest (Hungary) jun. 9-14. 1996.
Monduzzi Editore 173-176 (1996)

21. Kisely M., Molnár L., Tóth Á., Répássy G.: Rostasejtben elhelyezkedő lövedék eltávolítása endoscoppal
Fül-orr-gégegyógy. 42, 209-212 (1996)

22. Kisely M., Pócs E, Szűcs J., Tóth Á., Répássy G., Nemes Z.,: Soliter fibrosus tumor előfordulása az orrüregben
Fül-orr-gégegyógy. 42, 213-216 (1996)

23. Kisely M. : Adenoid vegetáció- Adenotomia
Háziorvos továbbképző szemle 3, 203-205 (1998)

24. Tóth Á., Kisely M., Sziklai I.: A Romberg-próba kvantitatív kiértékelése posturographiával
Fül-orr-gégegyógy. 45, 25-31 (1999)

25. Kisely Mihály, Tóth Ágnes, Emri Miklós, Lengyel Zsolt, Kálvin Beáta, Horváth Géza, Trón Lajos, Bogner Péter, Sziklai István: A vestibularis ingerület központi idegrendszeri feldolgozásának agyaktivációs vizsgálata pozitronemissziós tomográfiával, Orvosi Hetilap 141, 52, 2807-2813 (2000)

26. M. Kisely, Á. Tóth, M. Emri, Zs. Lengyel, G. Horváth, I. Sziklai, L. Trón: The effect of vestibular stimulation on the regional cerebral blood flow: Positron emission tomography study, 4th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery,
Berlin (Germany), May 13-18, 2000, Suppl.,

Editors: K. Jahnke, M Fischer, Monduzzi Editore, 42-53, (2000)

27. Répássy G., Hirschberg A., Rezek Ö., Kisely M., Tóth Á., Juhász A.: Supracricoid laterális gégeresectio a recessus piriformis rák kezelésére
Fül-orr-gégegyógy. 46, 155-162 (2000)

28. M. Kisely, Á. Tóth, M. Emri, Zs. Lengyel, B. Kálvin, G. Horváth, L. Trón, B. Bogner, I. Sziklai: Verarbeitung vestibulärer Impulse im Zentralnerversystem, HNO 49, 5, 347-354 (2001)
IF: 0.62

29. Kisely Mihály, Tóth Ágnes, Emri Miklós, Lengyel Zsolt, Kálvin Beáta, Horváth Géza, Bogner Péter, Sziklai István és Trón Lajos: Patológiás és indukált perifériás vestibularis egyensúlyzavar központi idegrendszeri hatása, Orvosi Hetilap 143, 21, suppl. 3, 1330-1332 (2002)

30. Emri Miklós, Bogner Péter, Balkay László, Tóth Ágnes, Kisely Mihály, Weisz Júlia, Ádám György, Glaub Teodóra, Berecz Roland, Repa Imre: [^{15}O] – butanol PET vizsgálatok térbeli standardizálása szegmentált, T1 – súlyozott MRI – felvételek segítségével, Orvosi Hetilap 143, 21, suppl. 3, 1249-1251 (2002)

31. Mihály Kisely, Miklós Emri, Zsolt Lengyel, Beáta Kálvin, Géza Horváth, Lajos Trón, László Mikó, István Sziklai, Ágnes Tóth: Changes in brain activation caused by caloric stimulation in the case of cohleovestibular denervation – PET study, Nuclear Medicine Communications 23, 967-973 (2002)
IF: 1.19

32. Miklós Emri, Mihály Kisely, Zsolt Lengyel, László Balkay, Teréz Márián, László Mikó, Ervin Berényi, István Szikilai, Lajos Trón, Ágnes Tóth.: Cortical projection of peripheral vestibular signaling, J. Neurophysiol (imprint) (2003)
IF: 3.15

LIST OF FREE PAPERS AND POSTERS

1. Kisely M., Rafic M.: A tűaspiráció helye a peritonsillaris abscessus diagnosztikájában és terápiájában.
DOTE Fül-Orr-Gégeklinika – Tudományos Ülése, 1990. okt. 01. DAB Székház

2. Tóth Á. Kisely M., Lampé I.: A vestibularis neuronitisről szerzett tapasztalataink (poster).
Nemzetközi Neurootologiai és Equilibriometriai Társaság XVIII. Kongresszus, 1991. Ápr.04-07. Budapest

3. Kisely M., Gombi R., Tóth Á., Lampé I.: Periodicus alternáló nystagmust okozó congenitalis cholesteatoma (poster).
Nemzetközi Neurootologiai és Equilibriometriai Társaság XVIII. Kongresszus, 1991.ápr.04-07. Budapest

4. M. Kisely, Á. Tóth, I. Lampé: Vestibular neoronitis reflected in rotatory test.

2nd European Congress of Oto-Rhino-Laryngology and Cervico-Facial Surgery, Sorrento (Naples) June 6-10th, 1992. (Abstr. Book, Monduzzi Editore, Bologna, 157-158, (1992)

5. Á.Tóth, M. Kisely, I. Lampé: Vestibular neuronitis reflected in caloric test.
2 nd European Congress of Oto-Rhino-Laryngology and Cervico-Facial Surgery, June 6-10th, 1992. (Abstr. Book, Monduzzi Editore, Blologna, 158, (1992)

6. I. Lampé, T.L.Rácz, L.Tóth, M.Kisely: Otoacustic emissions in normal and hearing impaired children
2 nd European Congress of Oto-Rhino-Laryngology and Cervico-Facial Surgery. June 6-10 th, 1992. (Abstr.Book, Monduzzi Editore, Bologna, 168, (1992)

7. Kisely M., Tóth Á.: Vízzel és levegővel történő caloricus ingerlés összehasonlítása. Magyar Fül-Orr-Gégeorvosok Egyesületének 34. Kongresszusa. Debrecen, 1992. aug. 26-29.

8. Tóth Á., Kisely M., Lampé I.: Our experiences about the use of vestibular index. XV. World Congress of Otorhinolaryngology Head and Neck Surgery. Istambul-Türkiye, 20-25 June 1993.

9. Kisely M., Tóth Á., Lampé I.: The comparison of the air and water caloric stimulation. XV. World Congress of Otorhinolaryngology Head and Neck Surgery. Istambul-Türkiye, 20-25 June 1993.

10. Kisely M ., Tóth Á., Lampé I.: Első tapasztalataink a vertikális rajzteszttel. Szimpózium a Magyar Fül-Orr-Gégeorvosok Egyesülete megalakulásának 100. Évfordulója alkalmából. 1993. Aug.27-28. Budapest

11. Tóth Á., Kisely M., Lampé I.: Stádiummeghatározás neurotinitis vestibularisban (Poster).
Szimpózium a Magyar Fül-Orr-Gégeorvosok Egyesülete megalakulásának 100. Évfordulója alkalmából. 1992. aug. 27-28. Budapest

12. M. Kisely, Á. Tóth, L. Rózsa, R. Gombi: About the oto-neurological symptoms of the cerebellopontine angle congenital cholesteatoma (poster).
Donasymposium Oto-Rhino-Laryngology 14-17. Sept. (1994) Salzburg

13. Tóth Á., Kisely M., Répássy G.: Az otoneurológiai vizsgálat számítógépes kiértékelése.
Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Szekciójának Ünnepi Vándorgyűlése, 1994. nov. 3-5. Budapest

14. Kisely M., Szabó G., Tóth Á., Répássy G.: Kombinált immunsupressiv therapia alatt észlelt sinusitis maxillaris kezelése gyermekkori kalcifikáló dermatomyositisben
Magyar Fül-Orr-Gégeorvosok Egyesülete Gyermek Fül-orr-gégészeti Kongresszusa, 1995. Május 11-13. Dobogókő

15. Tóth Á., Kisely M., Répássy G.: Romberg és Unterberger próba kivitelezhetősége gyermekkorban.

Magyar Fül-Orr-Gégeorvosok Egyesületi Gyermek Fül-orr-gége Kongresszusa, 1995. május 11-13. Dobogókő.

16. Dr. Tóth Á., Dr. Lampé I., Dr. Kisely M.: A tágult aquaeductus vestibularis syndromáról.
A Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyülése. 1995. okt. 26-28. Gyula

17. Dr. Kisely M., Dr. Tóth Á., Dr. Répássy G.: Szemelvények az intracranialis térfoglaló folyamatok cochleovestibularis leleteiből.
A Magyar Fül-Orr-Gégeorovosk Egyesülete Audiológiai Szekciójának vándorgyűlése. 1995. okt. 26-28. Gyula

18. Kisely M., Tóth Á., Répássy G.: The possibility of investigation of vestibulospinal system with CCG in children-normal values.
3rd Congress of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) June 9-14, 1996. Budapest, Hungary

19. Kisely M.: Differenciáldiagnosztikai érdekességek az otoneurológiában – Kisagy-híd szögleti tumorok.
Orvoslás és gyógyítás Kelet-Magyarország történetében a Honfoglalástól napjainkig. Nyíregyháza, 1996. jún. 24-27.

20. Kisely M., Tóth Á., Répássy G.: Az alsó- és felsővégtagi vertibulospinális reflexek objektív mérése.
Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Sectiojának Vándorgyűlése. 1996. okt. 24-26. Székesfehérvár.

21. Tóth Á., Kisely M., Répássy G.: Alkalmas-e a CCG a betegségfolyamat követésére?
Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyűlése. 1996. Okt. 24-26. Székesfehérvár.

22. Tóth Á., Márián T., Kisely M.: Mit nyújthat a PET a fül-orr-gégészetben?
Magyar Fül-Orr-Gégeorvosok egyesületének Tudományos Ülése 1997. Ápr.4. Budapest.

23. Kisely M., Jókay I., Répássy G.: Ionos protézis implantáció a hallócsontláncolat rekonstrukciójára.
Magyar Fül-Orr-Gégeorvosok Egyesületének Tudományos Ülése, 1997. Ápr.4. Budapest.

24. Tóth Á., Kisely M.: A luzerni mérőlappal szerzett tapasztalatainkról.
Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyűlése. 1997. Szept.25-27. Balatonfüred.

25. Kisely M., Tóth Á.: A vestibuláris rehabilitáció lehetősége.
Magyar Fül-Orr-Gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyűlése 1997.szept.25-27. Balatonfüred.

26. M.Kisely, Á.Tóth, L. Balkay, M. Emri, Zs. Lengyel, J. Kollár, Sz. Szakáll Jr., L. Trón: Positron emission tomographic examination of vestibular neuronitis patientes. 9th European Congress of Clinical Neurophysiology. Jun.3-7. 1998. Ljubljana, Slovenia.

27. Á. Tóth, M. Kisely, I. Sziklai: The role of posturography in the diagnostics of otoneurology. 9th European congress of Clinical Neurophysiology June 3-7. 1998. Ljubljana, Slovenia.

28. Kisely M., Tóth Á., Balkay L., Emri M., Lengel Zs., Kollár J., Szakáll Sz.Jr., Trón L., Sziklai I.: A vestibularis rendszer centralis projectiojának vizsgálata pozitron emissziós tomográfiával. Magyar Fül-Orr-Gégeorvosok Egyesületének 35. Kongresszusa. Pécs, 1998.jún.17-20.

29. Tóth Á., Kisely M., Sziklai I.: A posturogramok diagnosztikus értékéről. Magyar Fül-Orr-Gégeorvosok Egyesületének 35. Kongresszus, Pécs 1998. jún. 17-20.

30. Kisely M., Tóth Á., Sziklai I., Kollár J., Lehel Sz., Trón L.: A vesztibuláris ingerlés hatása a központi idegrendszerre. DOTE PET Centrum Tudományos Ülése Debrecen DAB Székház. 1999. febr. 22.

31. Kisely M., Kálvin B., Horváth G., Tóth Á., Sziklai I., Trón L.: A belső fül centrális kapcsolatainak vizsgálata pozitron emissziós tomográfiával. Öt éves a Magyar PET Program, Debrecen DAB székház, 1999. szept. 22.

32. Kisely M., Tóth Á., Szabó S., Sziklai I.: Ritka orr és orrmelléküregek elváltozások megoldása endoscoppal. Magyar Fül-Orr-Gégeorvosok Egyesülete Gyermek Fül-orr-gégészeti Szekciójának Vándorgyűlése. Székesfehérvár, 1999. okt. 14-16.

33. Kisely M., Tóth Á., Emri M., Lengyel Zs., Szikali I., Trón L.: The effect of vestibular stimulation on the regional cerebral blood flow: positron emission tomography study 4th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery, Berlin 2000. május 13-18.

34. Tóth Á., Kisely M., Valikovics A., Magyar T., Sziklai I.: The effect of vestibular stimulation on blodd flow velocity in the middle cerebral artery (Poster) 4th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery, Berlin 2000. május 13-18.

35. Kisely M., Tóth Á., Emri M., Trón L.: The changing of regional cerebral blood flow caused by caloric vestibular stimulation – PET study 10th European Congress of Clinical Neurophysiology, Lyon, France 2000. augusztus 26-30.

36. Tóth Á., Kisely M., Magyar T., Sziklai I.: A vestibularis stimuláció hatása a vérátáramlási sebességre az artéria cerebri médiában Magyar Fül-Orr-Gégeorvosok Egyesületének jubileumi, 36, Nemzeti Kongresszusa Hévíz, 2000. Október 24-28.

37. Kisely M., Tóth Á., Emri M., Szakáll Sz. Jr., Mikecz P., Trón L., Sziklai I.: A központi idegrendszer vérátáramlásának változása kalorikus vestibularis stimuláció hatására – PET tanulmány
Magyar Fül-Orr-Gégeorvosok Egyesületének jubileumi, 36, Nemzeti Kongresszusa Hévíz, 2000. Október 24-28.

38. Tóth Á., Kisely M., Emri M.: Central processing of the vestibular stimulation
Magyar Ideg-Elmeorvosok Társasága Nemzeti Nagygyűlése, Otoneurológiai Szekció Budapest, 2000. November. 16-18., Otoneurológiai Szekció November 18.

39. Kisely M., Bata L., Tóth Á.: Neurális cső záródási rendellenességének fül-orr-gégészeti vonatkozásai
A Magyar Fül-orr-gégeorvosok Egyesülete, Gyermek-fül-orr-gégész Szekciójának Kongresszusa, Balatonfüred, 2001. Május 17-19.

40. Gyuricza É., Jáger R., Kisely M.: Fül-orr-gégész és hematológus együttműködése gyermek fül-orr-gégészeti műtétek során
A Magyar Fül-orr-gégeorvosok Egyesülete, Gyermek-fül-orr-gégész Szekciójának Kongresszusa, Balatonfüred, 2001. Május 17-19.

41. Kisely M., Emri M., Trón L., Sziklai I., Mikó L., Tóth Á.: A caloricus vestibularis ingerlés mint komplex stimulus hatása a cerebrális cortexre
A Magyar Fül-orr-gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyűlése, Pécs, 2001. Szeptember 6-8.

42. Jáger R., Gyuricza É., Kisely M.: Veleszületett vérzékenységben szenvedő betegek gégészeti műtéteivel szerzett tapasztalatok
Magyar Thrombosis és Haemostasis Társaság Éves Tudományos Ülése, Alsópáhok, 2001. Szeptember 20-22.

43. Kisely M., Bobest M., Halász Gy., Tóth Á.: Harmonikus vestibularis tünetet okozó cerebellaris tumor
A Magyar Fül-orr-gégeorvosok Egyesülete Audiológiai Szekciójának Vándorgyűlése, Magykanizsa - Zalakaros, 2002. április 11-13.

44. Kisely M., Tóth Á., Emri M., Lengyel Zs., Horváth G., Sziklai I.: Modulation of the regional cerebral blood flow by peripheral vestibular disturbances. A positron emission tomography study
The XVIIth World Congress of The International Federation of Oto-Rhino-Laryngological Societies (IFOS), Cairo, Egypt, 28th Sept.- 3th Oct. 2002

45. Tóth Á., Emri M., Kisely M., Sziklai I.: Agytörzsi implantáción átesett betegek PET vizsgálata
Magyar Fül-, Orr-, Gégeorvosok Egyesülete 37. Nemzeti Kongresszusa, Siófok, 2002. Október 2-5

46. Halász Gy., Prugberger E., Csanaky Gy., Kisely M.: Krónikus laryngitis képében megbúvó tuberkulózis

Magyar Fül-, Orr-, Gégeorvosok Egyesülete 37. Nemzeti Kongresszusa, Siófok, 2002. Október 2-5

47. Kisely M., Emri M., Tóth Á.: A perifériás vestibuláris működés corticalis projekciója Magyar Fül-, Orr-, Gégeorvosok Egyesülete Tudományos Ülése, Budapest, 2003. Február 28.

48. Kisely M., Emri M., Lengyel Zs., Kálvin B., Horváth G., Trón L., Mikó L., Sziklai I., Tóth Á.: The vestibular and non-vestibular components of the caloric vestibular stimulus – A positron emission tomography stududy
30th Annual congress of the neurootological and equilibriometric society (NES), 2003. április 03-05. Portó, Portugália