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A 44 year old woman was admitted to our clinic because of progressive multiple sclerosis. One year before admission she had developed paresthesias of the legs, and subsequently of the arms. She became incontinent for urine and feces. She complained of numb feelings and muscle cramps in her legs. The medical history mentioned hypertension for which she used propranolol and hydrochlorothiazide. The family history was negative for multiple sclerosis. On examination there was vertical nystagmus, slight paresis of the legs, hyperreflexia, incoordination of the arms, and loss of sensation from a mid-thoracic level. The tendon reflexes of the legs were very brisk, and both plantar responses were extensor. Examination of CSF showed eight white cells/mm$^3$ (all lymphocytes), and an immunological production of IgG and IgM. Brain MRI and the cervical part of the spinal cord showed multiple white matter lesions. Additional investigations excluded other diseases—for example, borborexiosis and lupus erythematosus. A 10 day treatment with daily administration of 1000 mg intravenous methylprednisolone was started. Methylprednisolone was given in its injectable form, methylprednisolone sodium succinate, which hydrolyses to methylprednisolone in the body. The infusion period was one hour. Because of cystitis she was also received trimethoprim. One day after the intravenous infusion, when the course had ended, the patient developed generalised urticaria which disappeared after a few days, and which could have been induced by either drug. After informed consent of the patient it was decided to give another course, as the intravenous methylprednisolone course improved her multiple sclerosis. To guarantee minimal risk, we gave 1000 mg intravenous methylprednisolone under close monitoring. After the first infusion there was a reactivation of the skin rash, and difficulty with swallowing and breathing, suspicious of an anaphylactic reaction. We gave methylprednisolone intravenously, after which the symptoms immediately resolved. Because of clinical improvement, therapy was continued with a 1000 mg dose of intravenous methylprednisolone divided into two, again under close monitoring. No symptoms developed. The next day we gave the drug again close after which the patient developed dyspnoea. We waited two days and reintroduced intravenous methylprednisolone therapy in divided doses. After the second dose the patient again became short of breath, needing 4.0 mg intravenous clemastine. We decided to give the patient the next two doses of 500 mg intravenous methylprednisolone followed by 4.0 mg intravenous clemastine, and no symptoms developed.

A skin reaction and histamine release test were performed to elucidate the pathogenesis of the allergy. The patient showed a skin reaction of 5.5 mm after subcutaneous injection of methylprednisolone (1.0 ml 5% methylprednisolone in isotonic saline). How­

Anaphylactoid reaction to intravenous methylprednisolone in a patient with multiple sclerosis

Exacerbations in multiple sclerosis are treated with short courses of high dose intravenous methylprednisolone. Treatment with intravenous methylprednisolone has mainly minor side effects such as transient flushing, a brief disturbance of taste, insomnia, and mild weight gain. An anaphylactoid reaction after intravenous methylprednisolone treatment has been described in only one patient with multiple sclerosis. We report on a patient with multiple sclerosis who developed an anaphylactoid reaction on high dose intravenous methylprednisolone treatment. Additional investigations were performed to elucidate the mechanism of this reaction to intravenous methylprednisolone.
CORRESPONDENCE

Unilateral auditory hallucinations: ear or brain?

Brasic and Perry convincingly describe a boy with unilateral otopathic auditory hallucinations. However, their literature review is very much incomplete. Four CNS causes for auditory hallucinations other than from a hyperactive ear. They also do not cite a misleading, postulating dubious CNS causes. However, their literature review is very much incomplete. Four CNS causes for auditory hallucinations other than from a hyperactive ear. They also do not cite a misleading, postulating dubious CNS causes.

Their next three references supposedly show that auditory hallucinations are caused by stimulatory phenomena in the CNS—namely, epilepsy (Keshavan et al, 1992), schizophrenia (Silbersweig et al, 1995), and drugs (Ketter et al, 1996). Keshavan et al reviewed musical hallucinations. In epilepsy, they discussed six cases from Heinrich Brücke in whom music occurred as part of an epileptic aura, four of whom had concomitant ear disease; three case reports without structural brain lesions, two with pronounced deafness, the third with attacks of nausea and rotary vertigo but no neurotological investigations; three of Penfield's cases were from one ear, but no ear or hear­ing examination. In one of these last three, seizures were of a "new and curious type", including deafness, unilateral voices, and music, starting two years after tumour removal. Far from implicating the brain, this review of musical hallucinations strongly implicates the ear. Even if epileptic patients are not known to have ear disease, this should be suspected, as Jackson and Gowers established last century that epilepsy can arise from the ear.

In their PET study on hallucinating schizophrenic patients, Silbersweig et al found increased blood flow in the thalamus and not the occipital. This is not evidence that auditory hallucinations are generated in the brain; instead, it is consistent with peripheral impulses funnelling up via the thalamus.

The volunteers of Ketter et al consistently (29 out of 32 subjects) reported procaine induced auditory hallucinations (unformed buzzing, ringing, or electronic sounds). They considered procaine a selective limbic activator, even though no change in cerebral blood flow corresponded to the "auditory hallucinations". In an ear, nose, and throat clinic the above noises would definitely be labelled tinnitus, and an obvious peripheral cause usually found. In line with this, procaine causes cochlear hyperactivity (increased wave I and II amplitude in dogs); in view of the link between epilepsy and the ear, it is noteworthy that the EEG changed from an awake pattern to seizure activity.

The 1988 review of sensory deprivation by Perlerta et al was cited as an example of auditory hallucinations from sensory disinherit. I reviewed some of this literature, concluding that for musical hallucinations there is as much evidence for ear disease and laryn­thine hyperactivity as when they occur in all other conditions and diseases. Deprivation is a peripheral sensor; inner ear and peripheral white noise is used to mask environmental sounds, whereas if all background noises are reduced, normal subjects will start to have tinnitus. I recently tested a 16 year old dyslexic patient who had never known silence through it), yet had never complained of auditory hallucinations. Sensory deprivation is more likely than deprivation, as in fact misprinted!

A similar case to that of Brasic and Perry throws considerable light on pathophysiologi­cal processes involved. Both were tormented by voices of devils, having symptoms of unilateral ear disease; saw their environment changing; had fiery visions (fire surrounded by cockroaches, devil transforming into burning wisp of straw); possible fluid in one middle ear (blocked grommet plus air-bone gap; fatty discharge from one ear). Conspicuously omitted was any mention of tinnitus, the most likely geriatric of the auditory hallucinations. Fortunately, the other case was Martin Luther, who clearly described ringing in his ears, unendurable buzzing, thundering, cracks, thumps, etc. Once, he had a musical hallucination (bells of specific church bells) which woke him in bed because of noises in his head. Curiously, Luther did not have a simple demonic or religious explanation for his torments. Instead he blamed Satan for his Meniere's symptoms (headache, episodic vertigo, tinnitus), which in turn he recognised caused his hallucinations. In fact his symptoms were typical of post-oto­pathic musical hallucinations. There is no better evidence that he had "French disease". If Brasic and Perry still assert a CNS origin for auditory hallucinations they need an original case report, not reviews or secondary sources. Repeated appeals for non-otological neurological musical hallucinations have failed (suggested cases with brainstum prices were also deat). I would now like to broaden the challenge to cover auditory hallucinations as well. Unless someone can come up quickly with a case of auditory hallucination due to a clear neurological lesion in someone with normal ears and hearing, the only proved cause of auditory hallucinations is otological.

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Brasic and Perry reply:
Gordon conjectures that otopathological pathology is the necessary and sufficient condition for auditory hallucinations. We disagree. We hypothesise that auditory hallucinations have many aetiologies which can be classified as otological, neurological, neuropsychiatric, and combined. Auditory hallucinations may result from the multiple effects of otopathological, such as altered signal transduction in hair cells. For example, in response to minimal environmental stimuli, diseased cochlear hair cells may generate random frequencies producing white noise perceived as tinnitus in some persons. Auditory hallucinations may also result from neurological illnesses, including after right temporal lobectomy for intracerebral hemorrhage without seizures. We are preparing a manuscript on auditory hallucinations in neurological disorders. Auditory hallucinations due to neuropsychiatric disorders are being studied, particularly in schizophrenia. On functional MRI, two patients with schizophrenia experiencing auditory hallucinations showed decreased responses of the temporal cortex to external auditory stimulation. Therefore, auditory hallucinations in some patients with schizophrenia may correspond with maximal activation of the auditory association cortex. The physiology of thinking in words was assessed utilizing PET in six persons with schizophrenia who experienced auditory hallucinations, six persons with schizophrenia...