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This is the first demonstration of neuromyotonia in a genetically engineered animal model of a hereditary neuropathy with a defined gene defect. Our finding may eventually help to define the pathogenesis and mode of treatment of hereditary forms of human neuromyotonia.

US was supported by a grant from the Swiss National Science Foundation and KVT and JZ by University funds.

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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 disruption of taste, insomnia, and mild weight gain. Anaphylactoid reaction after intravenous methylprednisolone treatment has been described in only one patient with multiple sclerosis.1 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.

A 44 year old woman was admitted to our clinic because of progressive multiple sclerosis. One year before admission she had developed paresthesia of the legs, and subsequently of the arms. She became incontinent for urine and faeces. She also 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 paresthesia of the fingers and legs, 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 the skin rash, and difficulty with swallowing and breathing, suspicious of anaphylactic reaction. The clinical reaction is possibly due to anaphylaxis. The histamine release tests are unreliable as they also gave positive reactions in the healthy volunteers.1,2 Allergic reactions to oral or intravenously administered corticosteroids in patients have been found but occur infrequently (0.3% of the patients).3 Risk factors for developing allergic reactions after receiving intravenous methylprednisolone are asthma and aspirin intolerance.4 Our patient had no history of asthma or otherwise.

Skin tests have been used to investigate the nature of side effects to intravenous methylprednisolone.5 We showed that skin tests are unreliable as they also gave positive reactions in the healthy volunteers. The "allergic" reactions are probably not based on an IgE mediated reaction, but could have been caused by fast administration of methylprednisolone leading to high plasma concentrations. However, raised concentrations were not found.6 The histamine release reaction for methylprednisolone sodium succinate was not indicative of an IgE mediated reaction because we did not observe a histamine release due to a (dose related) toxic effect of methylprednisolone on the basophil granulocytes.

In conclusion, the clinical symptoms which developed during high dose intravenous methylprednisolone are rare, but can be dangerous. Therefore, patients with multiple sclerosis who receive an intravenous methylprednisolone treatment for the first time should be carefully monitored. According to this case the mechanism of the reaction seems to be IgE independent, and may have been induced by toxic concentrations of methylprednisolone on the basophil granulocytes. Skin testing with methylprednisolone is unreliable, and should be interpreted with care.7

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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 weighted towards non-otological CNS causes for auditory hallucinations other than from a hyperactive ear. They also do not cite a relevant prior case.

Their paper starts: "Unilateral auditory hallucinations...are associated with contralateral CNS lesions". Their only supporting reference is to Toulouse, who reviewed four adults with neurological disease and unilateral auditory hallucinations, allegedly of cortical origin. These turned out to be anything but. One case (Regis, 1881) had voices in his left ear aggravated by alcohol, sounds of a bell and water in his right; impaired hearing in his left ear (thought by Toulouse to be of cortical origin); the 1888 case had bilateral auditory hallucinations, worse on the left, abolished by blocking off the ear which was full of pus; the third case was an alcoholic wine merchant, heard voices in her right ear, and had bilateral deafness from his right ear, but there was no examination of the ear. 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 implies 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, Silverstein et al found increased blood flow corresponding 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 ISC, they found cochlear hyperactivation (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 1968 review of sensory deprivation by Peters et al was cited as an example of auditory hallucinations from sensory disinhibition. I reviewed some of this literature, concluding that for musical hallucinations there is as much evidence for ear disease as for hearing loss. We disagree. We are preparing a manuscript concerning auditory hallucinations in neurological disorders. Auditory hallucinations due to neurogenic causes may result from the multiple effects of otopathology, such as altered signal transduction in hair cells. For example, in response to minimal environmental stimuli, disturbed hair cell function may be producing white noise perceived as tinnitus in some persons. Auditory hallucinations may also result from neurological illnesses, including after right temporal lobectomy for refractory epilepsy.

Brasic and Perry reply: Gordon conjectures that otological 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 otopathology, such as altered signal transduction in hair cells. For example, in response to minimal environmental stimuli, disturbed hair cell function may be producing white noise perceived as tinnitus in some persons. Auditory hallucinations may also result from neurological illnesses, including after right temporal lobectomy for refractory epilepsy.

We are preparing a manuscript concerning 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 reduced blood flow in the cortex. 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.