ictal events confirmed the right hippocampal origin of the seizures.

Subsequently, temporal lobectomy was performed on 12 October and the right hippocampus was removed from the tip to 1·5 cm posteriorly. Ammon's horn sclerosis was confirmed in the excised tissue. Several days after the operation, however, he became increasingly euphoric and elevated in mood. His speech was raced. He incessantly interrupted conversations around him. He became a constant joker. At the 20th day after the lobectomy, this mood change culminated in sexual disinhibition and sporadic explosive behaviour, which necessitated a two week stay in a psychiatric hospital. Throughout this episode, which lasted about two months, he was alert and fully oriented and the EEG recordings showed frequent right temporal spikes. Four consecutive EEG documentations registered within three months after the lobectomy showed this elevated excitability in the right mid-temporal region. These spikes had disappeared completely by the next February when his mood was stabilised to the level of the presurgical period. No spikes were found in three further EEG recordings registered in the subsequent 12 months. No change in medication was made after the operation. His epilepsy was relieved after the operation. There was no history of psychiatric illness before the operation.

Depression has been one of the well known psychiatric manifestations after temporal lobectomy. Hill *et al*[3] noted in the late 1950s that aggressive acting out, one of the well recognised personality trends in a group of patients with temporal lobe epilepsy, was often switched to depressive seclusion after operation. They designated this replacement of preoperative aggressive hostility with postoperative depressive withdrawal as a "turning in" of aggression. By contrast with this longstanding recognition of postoperative depression, hypomanic states arising after temporal lobectomy do not seem to have been mentioned in the medical literature. Indeed, Mace *et al*[1] pointed out in a discussion on de novo psychoses that affective symptoms were most evident in those cases when they appeared early after surgery. Although this was also true of the affective psychosis in the current case because it appeared within a few days of the lobectomy, it should be noted that the affective symptoms in all the cases noted by Mace *et al*[1] were dominated not by elevated but by depressed moods. Reports of five cases with postictal hypomania by Barczak *et al*[4] and by Byrne[5] challenged the prevailing view that hypomania was not (or only scarcely) found in close relation to epilepsy. This case report of a hypomanic state as a de novo psychosis after operation is another example supporting the link between the hypomania and epilepsy.

An increased temporal spike activity concomitant with psychiatric symptoms was found in the current case. The clinical course of the hypomanic mood swing corresponded well with the fluctuation in the EEG findings. As long as the hypomania dominated the clinical setting, clusters of right mid-temporal spikes were recorded in the repeated EEG. This suggested that an increased excitability in the residual tissue immediately after the lobectomy may play some part in the genesis of postoperative psychoses. The short interval between the operation and the psychiatric manifestation also supported this view.

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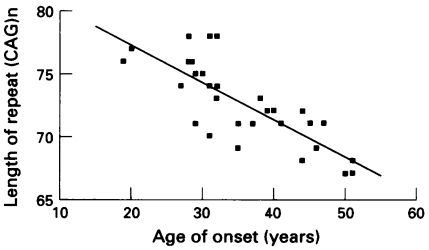
Machado-Joseph disease mutations as the genetic basis of most spinocerebellar ataxias in Germany

Machado-Joseph disease is an autosomal dominant inherited neurodegenerative disorder pathologically characterised by neuronal loss and gliosis in the cerebellum (especially the dentate nucleus), the spinal cord (spinocerebellar tracts, anterior horn cells, posterior columns, and Clarke's columns) and to varying degrees in the substantia nigra, the subthalamic nuclei, cranial motor nuclei, and peripheral nerves. Clinically Machado-Joseph disease presents with a broad range of symptoms including variable combinations of cerebellar ataxia, pyramidal and extrapyramidal features, peripheral neuropathy, progressive external ophthalmoplegia, and faciolingual fasciculation.[1] Machado-Joseph disease was originally described in Portuguese-Azorean descendants and has rarely been encountered in ethnic groups other than Portuguese.[1] Up to now, no patients with the clinical diagnosis of Machado-Joseph disease have been reported in Germany. Recently, the Machado-Joseph disease gene locus has been mapped to chromosome 14q and the disease causing mutation has been identified as an unstable and expanded $(CAG)_n$ trinucleotide repeat.[2]

We investigated the Machado-Joseph disease mutation in 38 families with dominant cerebellar ataxias and in 21 patients with sporadic forms of ataxia of German ancestry. In 19 of 38 families an expanded trinucleotide repeat in the Machado-Joseph disease gene has been identified. Analysis of the $(CAG)_n$ repeat length and the age of onset disclosed an inverse correlation, with the longest repeats in patients with juvenile onset (figure). None of the sporadic patients carried the Machado-Joseph disease mutation indicating that new mutations occur rarely.

Prominent clinical features of the German patients with ataxia and bearing the Machado-Joseph disease mutation (table) included cerebellar symptoms such as ataxia of limbs, gait, and stance, dysarthria and cerebellar oculomotor disturbances, and a varying combination of dysphagia, spasticity, and peripheral neuropathy with amyotrophy and sensory loss. Characteristic signs of Machado-Joseph disease as described in patients of Portuguese or Japanese descent, such as dystonia, extrapyramidal rigidity, faciolin-



Correlation between the expanded (CAG)n repeat length in the Machado-Joseph disease gene and the age of onset in patients with spinocerebellar ataxia type 3/Machado-Joseph disease. The regression curve derives from the formula: trinucleotide size = 83·3 − 0·3 × age of onset (r = − 0·79, P = 0·00000025).

Clinical characteristics of patients with (SCA3), (MJD), and (SCA1)

	SCA3/MJD Germany†	*MJD USA*[4]	*MJD Japan*[5 6]	*SCA3 France*[3]	*SCA1 Germany‡*
No of families	19	?	1	2	4
No of patients	30	25	12	18	8
Age of onset (mean (SD)) (y)	37 (7)	36 (17)	31 (10)	33 (7)	37 (4)
(range) (y)	(19–51)	(10–64)	(20–44)	(20–47)	(32–47)
Disease duration (mean (SD)) (y)	12 (5)	12 (7)	11 (5)	10 (6)	8 (4)
Clinical signs (%):					
Cerebellar: gait ataxia	100	100	?	?	100
Limb ataxia and dysmetria	97	92	?	?	100
Dysarthria	90	96	?	?	100
Cerebellar oculomotor signs	93	96	?	?	88
Pyramidal: spasticity	57	52	?	?	50
Increased tendon reflexes	40[b**]	64[f*]	92[h**]	33	13
Extensor plantar responses	40	64[f*]	58	50	13
Extrapyramidal: rigidity	13	40	25	11	0
Dystonia	3[a***,b***]	36[e*]	67[g***,h*]	6	0
Amyotrophy	23	32	42[g*]	11	38
Decreased vibration sense	70[a***,b***]	36[f**]	8[h***]	44[i*]	100
Ophthalmoplegia	37	?	58	39	38
Faciolingual fasciculation	10[a***,b***]	56[d*,e***]	100[g***,h*]	0	25
Dysphagia	63	?	?	?	63
Dementia	10c*	?	8		25

*P < 0·05; **P < 0·01; ***P < 0·001 comparison of percentages with a corrected χ^2 test.
a: comparison between SCA3/MJD Germany and MJD USA; b: SCA3/MJD Germany and MJD Japan; c: SCA3/MJD Germany and SCA1 Germany; d: MJD USA and MJD Japan; e: MJD USA and SCA3 France; f: MJD USA and SCA1 Germany; g: MJD Japan and SCA3 France; h: MJD Japan and SCA1 Germany; i: SCA3 France and SCA1 Germany. †Data presented in this paper. ‡Schöls *et al*, unpublished data.

gual fasciculations, and bulging eyes, were rare in German patients.

The clinical profile of the German patients bearing the Machado-Joseph disease mutation is indistinguishable from that of French families described as having spinocerebellar ataxia type 3 with a gene locus on chromosome 14q in the vicinity of the Machado-Joseph disease gene.[3] Spinocerebellar ataxia type 3 and Machado-Joseph disease were considered to be independent diseases, however, because of clinical differences. Identifying the Machado-Joseph disease mutation in German patients with the spinocerebellar ataxia type 3 phenotype provides good evidence for the hypothesis that Machado-Joseph disease and spinocerebellar ataxia type 3 are caused by alterations of the same gene.

With this initial study we show that the Machado-Joseph disease mutation is of major diagnostic importance as it is responsible for about 50% of dominant ataxias in German families although Machado-Joseph disease has not been described in Germany before.

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Oculographic findings in traumatic unconsciousness: prognostic implications

The analysis of saccadic eye movements can assist in the diagnosis and anatomical localisation of several neurological and psychiatric disorders. Spontaneous and reflexive eye movements may also be of value in the neurosurgical assessment of traumatic brain injury. Organised spontaneous eye movements require integrity of the brain stem, and some reflexive movements need reciprocal connections with visual and auditory cortical centres. Traumatic brain injury results in a graded centripetral disconnection of cortical and subcortical structures in a rostrocaudal direction.[1] Much of the mortality and morbidity associated with head injury is thought to be due to neural disconnection caused by diffuse axonal injury.[1] Taking advantage of the standing corneoretinal potential of the eye, it is relatively easy to record orbital movements electrographically with periorbital electrodes.[2] Ocular microtremor, which is due to the constant tonic input of brain stem oculomotor centres, has been correlated with the clinical state of comatose patients and related to prognosis.[3]

With informed consent from the next of kin, we prospectively studied the electro-oculograms of 60 comatose patients (47 male and 13 female; age range 1 to 80, mean 36·4 (SD 19·10) years) after severe, non-penetrating head injuries (range one to 23 days postinjury, mean 3·2 days). All patients were sedated with propofol (1·0 to 3·0 mg/kg/h) and morphine (0·02 to 0·15 mg/kg/h), and mechanically ventilated to maintain a $PaCO_2$ of about 35 mm Hg. Spontaneous and auditory reflexive eye movements were recorded electrographically from bipolar pairs of periorbital silver/silver chloride electrodes, attached to the infraorbital margins referenced to F7 and F8 (international 10/20 system of electrode placement), with a paper speed of 30 mm/s, gain of 50 μV/cm, and filter bandwidth of 0·3 to 35 Hz. The spontaneous and reflexive saccadic eye movements to speech (a greeting and the patient's first name) were assessed by visual inspection of the oculogram and graded according to abnormality. When present and conjugate the saccades were classified as "normal"; when present but dysconjugate they were classified as "asymmetric"; and no movement on the oculogram was classified as "absent". In 35 patients (58·3%) the saccades were judged to be normal, in 15 (25·0%) they were asymmetric, and in 10 (16·7%) they were absent (table). The patient's Glasgow coma scale scores were determined at the same time, and they correlated with the oculogram grading (Spearman's correlation coefficient, r_s = 0·37, P = 0·007). Patient outcome was assessed by personal interview at three months on the five point Glasgow outcome scale (table 1). Sixteen patients (26·7%) died, five (8·3%) were in the vegetative state, 17 (28·3%) were severely disabled, 14 (23·3%) were moderately disabled, and eight (13·3%) had made good recoveries. There was a good correlation between oculogram grade and outcome category at three months (r_s = 0·50, P = 0·0003). Of the ten patients without electrographic eye movements seven died, all of whom had histopathological evidence of diffuse axonal injury involving the upper brain stem; the absence of eye movement is therefore significantly associated with non-survival (χ^2 = 11·52, P = 0·001).

Oculogram grade against three month Glasgow outcome scale (GOS)

	Oculogram		
	Normal n (%)	*Asymmetric n (%)*	*Absent n (%)*
GOS:			
Dead	4 (6·7)	5 (8·3)	7 (11·7)
Vegetative state	3 (5·0)	1 (1·7)	1 (1·7)
Severely disabled	11 (18·3)	5 (8·3)	1 (1·7)
Moderately disabled	11 (18·3)	2 (3·3)	1 (1·7)
Good recovery	6 (10·0)	2 (3·3)	0 (0)

It is well known that eye movements have prognostic significance in brain injury, in particular when spontaneous and reflexive movements are absent, suggesting midbrain and brain stem dysfunction respectively.[4] Indeed the clinincal categorisation of eye movement has been used in the Innsbruck coma scale for predicting non-survival after head injury.[5] This simple electrodiagnostic test and classification allows quantification of eye movements, and may assist clinicians in the objective prediction of outcome after severe, coma producing traumatic brain injury. It is relatively easy to include the technique as part of the routine prognostic electrophysiological assessment of cerebral function, and it does not have some of the limitations or risks associated with eliciting oculocephalic and oculovestibular reflexes in patients with trauma affecting the cervical spine or tympanic membrane. The test cannot supplant clinical diagnosis, however, as in our experience its sensitivity is only 43·7% and its specificity is 93·2%, and we do not know exactly how eye movements are affected by the level of consciousness. Because spontaneous and reflexive eye movements require an intact neural circuitry, we suggest that their asymmetry or loss reflect increasingly extensive neural dysfunction or disconnection. It is possible that widespread diffuse axonal injury may provide the pathological substrate for this loss of functional integrity.

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Limbic system dysfunction in Alzheimer's disease

Positron emission tomography studies of cerebral glucose metabolism in Alzheimer's disease have shown a pattern of hypofunction in temporal, parietal, and frontal lobes