nystagmus, dislocation of the left lens in the vitreous humour, and multiple retinal atrophic lesions were also found.

An IQ of 49 was found on the Wechsler adult intelligence scale. The neurological clinical examination showed cerebellar ataxia with limb and truncal ataxia and ataxic gait; also in this patient, mild hypotonia of the lower limbs, brisk tendon reflexes, and Babinski’s sign on the left side were present. Speech was syllabic, poor, and atecholalic.

Brain MRI showed a pronounced reduction in size of the vermis and of the cerebellar hemispheres and a mild cerebral cortical atrophy. An ECG was characterized by a slow background activity (6 Hz). No signs of muscular or peripheral nervous system involvement were found on EMG.

Routine blood and urine analysis, lysosomal activity, and renal and urinary aminoacids and rautometabolic screening were normal. Karyotype was 46, XY and the molecular analysis for the FMR1 gene was normal.

These two patients represent a difficult diagnostic problem. They show common features such as congenital ataxia, nystagmus, mental retardation, and ocular abnormalities (retinal atrophic changes) which make it difficult to include them in one of the groups already proposed. In particular, the Gillespie syndrome is defined by the association of partial aniridia, congenital cerebellar ataxia, and mental retardation. Our patients were both affected by different ocular abnormalities such as retinal atrophic lesions and nystagmus. Additionally, one of them also had keratoconus, for which surgical treatment was needed and the dystrophic changes of the iris reported above only occurred after the surgical manipulation of the eyes.

For these reasons, we think that our patients are a new example of the consider- able clinical and genetic heterogeneity which characterise congenital cerebellar ataxia. Also, the family tree of our patients does not allow us to reach a conclusion on the mode of inheritance of the disorder, even if the strict consanguinity of the parents strongly suggests the possibility of an autosomal recessive inheritance.

It seems important to underline that the patients with congenital ataxia described in the previous literature are usually of a much younger age than our two brothers and that the memory loss reported in the brothers could represent the first symptom of a true dementia process, for which monitoring will be necessary in the future. In fact, even if no assessment of the cognitive status was performed before, our patients had presented a stable psychomotor picture before the develop- ment of memory loss. Thus memory loss and dementia usually long term complication of cerebellar ataxia syndromes.

In conclusion, we suggest that our patients may represent a new combination of congenital cerebellar ataxia, mental retardation, and atrophic retinal lesions. This might constitute a new clinical entity if similar patients are found in the future.

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Stimulation single fibre EMG study in a patient with Schwartz-Jampel syndrome

Schwartz-Jampel syndrome is a rare congenit- al disorder characterised by short stature, oculo-facial abnormalities, bone and joint deformities, clinical myotonia, and persist- ent spontaneous activity. Lehmann-Horn and colleagues1 showed two muscle mem- brane abnormalities in Schwartz-Jampel syn- drome. By voltage clamp and patch clamp techniques. The abnormalities included reduced Cl conductance and synchronised late opening of Na channels. These findings indicate that the origin of the spontaneous activity in Schwartz-Jampel syndrome is located in the muscle membrane itself. However, some reports suggested that the origin of the spontaneous activity may be found in the nerve or end plate because stimulation SFEMG in or patient with these activities. Single fibre EMG (SFMG) has been widely employed to study the involve- ment of nerve or neuromuscular transmis- sion. However, difficulty is anticipated during jitter measurement in Schwartz-Jampel syndrome because the spontaneous involuntary activities may be elicited during voluntary muscle contraction. We employed stimulation SFEMG in or patient with Schwartz-Jampel syndrome in an attempt to obtain a more precise assessment of the neu- romuscular transmission. We are unaware of any previous application of this technique in Schwartz-Jampel syndrome.

The patient was a 27 year old woman diagnosed as having Schwartz-Jampel syn- drome. She presented clinically with short stature, ocular abnormalities, joint and skeletal deformities, percussion and action myotonia, and hypoactive deep tendon reflexes. Concentric needle EMG (CNEMG) performed when the patient was 13 years old disclosed spontaneous activity evoked by needle movements and muscular contraction that persisted at rest. Neither cold nor lidocaine suppressed the spontane- ous activity, but it was suppressed by local ischaemic exercise. The following electro- physiological studies were done: (1) routine muscle, sensory, and facial nerve conduction study (CSF; at 3 Hz) routine ulnar nerve stimulation; (2) rou- tine CNEMG; (3) voluntary SFEMG; (4) stimulation SFEMG. Routine nerve conduc- tion studies, repetitive nerve stimulation, and EMG (Counterpoint software, Dantec Corp, Denmark) were performed with concentric needle electrodes (Medelec CN-35, UK) and single fibre electrodes (Medelec SF-25, UK). Stimulation SFEMG was performed at the extensor digitorum communis muscle, which showed spontaneous activities without any weakness according to standard methods. Stimulation frequency was set at 5 Hz.

Routine nerve conduction studies that included measurement of distal latencies, conduction velocities, and amplitudes of compound muscle action potentials (MCP) and sensory nerve action potentials (SNAP) in the upper and lower limbs were normal. Repetitive ulnar nerve stimulation at 3 Hz showed no significant decrement of ampli- tude and area of CMAPs. CNEMG showed no needle insertional myotonic discharges and mild muscular contraction induced two types of spontaneous activity which per- sisted even at rest. One type of spontaneous activity was typical myotonic discharges that showed increment and decrement of firing rates and amplitudes. The maximal firing rate was 100 Hz and the duration of the myotonic run was about 10 seconds. Another type of spontaneous activity was high frequency biphasic simple discharges that did not show variations of frequency and amplitudes, and that had a firing rate of about 50 Hz and a duration of 10-30 sec- onds. Fibbrilations were rarely seen. Precise analysis of motor unit potentials (MUPs) were difficult because of interference from spontaneous activities. Among those MUPs were identified, the durations were either normal or slightly increased. Fibre SFEMG during voluntary contraction showed that most of the spontaneous activity consisted of single muscle fibre action potentials, differ- ently from a complex repetitive discharges (CRDs), and frequent occurrence of extradischarges. Although jitter and fibre density measurements by voluntary SFEMG were difficult to perform due to the influence of spontaneous activities, a few jitter values found measurable without interfer- ence by spontaneous activity were normal. On stimulation SFEMG, we were able to perform jitter measurement of 21 units, and although spontane- ous activity was not completely eliminated by electrical stimulation sometimes interfered. On occasions of interference by spontaneous activity, the jitter seemed to be increased. We performed SFEMG without spontaneous activity only (figure). The mean jitter values (19.0 ± 2 Hz 14-2 (6-6) μs) and individual jitter values were normal except in one end plate. The electrophysiological examination of the present case of Schwartz-Jampel syndrome are summarised as follows: (a) normal normal nerve conduction studies; (b) no abnormal decre- ment in any repetitive nerve conduction; (c) spontaneous activity of typical myotonic dis- charge and atypical myotonic-like discharge but not CRD, and (d) normal neuromuscu- lar transmission. Based on these electro-
Physiological studies, the nerve does not seem to be the origin of spontaneous activities in our patient. Pharmacological studies support this hypothesis. Stimulation SFEMG confirmed a normal neuromuscular transmission in Schwartz-Jampel syndrome, whereas voluntary SFEMG was not helpful due to technical difficulties.

Jitter studies have been performed in three previous reports of Schwartz-Jampel syndrome. However, adequate numbers of single fibre action potential pairs for quantitative measurement were not obtained in these studies. Their data showed abnormal jitter with rapid blocking. In one case, electrophysiological and morphological studies, including a quantitative end plate measurement, suggested no abnormalities in the nerve and end plate despite the presence of an abnormal jitter. The jitter with voluntary SFEMG can be derived not only from the involvement of nerve and end plate but also from the muscle itself. The so-called ‘myogenic jitter’ is usually due to interdischarge interval (IDI) dependent jitter which results from the velocity recovery function (VRF). The main causes of irregularity of IDI is the irregularity of MUP firing and is enhanced by large differences of propagation velocity induced by differences of muscle fibre diameters (for example, hypertrophy of muscle fibres in Schwartz-Jampel syndrome). In instances when spontaneous activity and extrasynchrony occur, irregularity of IDI may be even more pronounced. Stimulation SFEMG, on the other hand, does not produce IDI dependent jitter because of a steady stimulus frequency. An exercise of caution is needed during jitter measurement should there be spontaneous activity, interference of MUP, or extra discharges as these may change IDI due to supernormal VRF.

The present stimulation SFEMG study, with a careful analysis, showed normal end plate function and strongly supports the hypothesis that the origin of spontaneous activities in our patient with Schwartz-Jampel syndrome is in the muscle itself.

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Apolipoprotein E polymorphism and late onset Alzheimer's disease in Argentina

Several genes and, possibly, environmental factors are involved in the initiation, progression, and severity of Alzheimer's disease (AD). The inheritance of the three common Apolipoprotein E (APOE) alleles (e2, e3, and e4) can induce a differential individual susceptibility to Alzheimer's disease.

There is a large body of evidence showing that the e4 allele of APOE is a genetic risk factor for late onset of Alzheimer's disease in an allele dose dependent manner.

The e4 allele frequency varies with the ethnic background as inferred from Japanese and Spanish studies, in which values for the general population are lower than those from the United States, Canada, and northern European countries. The e4 frequencies reported range from 0.24 to 0.52 in patients with Alzheimer's disease, 0.06 to 0.18 in controls, and 0.1 to 0.2 in the general population regardless of the prevalence of Alzheimer's disease in each country (for review see Adrover et al.).

As little is known about the e4 allele frequency and Alzheimer's disease in Hispanic people from South America, we conducted a case-control study in Argentina. The aim of our work was to evaluate the association between the APOE allele genotype and late onset Alzheimer's disease in a population with a heterogeneous genetic background due to the fusion of South American Indian natives with northern and southern European immigrants.

We studied 45 patients (mean age 74.72 (SD 5.5) years, mean age of onset 69-61 (SD 4.7) years) with a diagnosis of probable Alzheimer's disease according to NINCDS-ADRA criteria. Sporadic patients were defined as those with no first or second degree relatives with dementia in at least two generations back. The 45 age matched controls (mean age 71-89 (SD 7-2) years) had a normal neuropsychological evaluation and no history of psychiatric disorders or alcoholism. In addition, we studied 101 healthy blood donors younger than 50 years (mean age 33-81 (SD 8-5) years) to determine the e4 allele frequency in the general population. All the subjects included in the study were Hispanic and at least the second generation of native Argentines. The study protocol and informed consent from all subjects or their relatives was approved by the institution's ethics committee.

Genomic DNA was obtained from peripheral blood by standard procedures and APOE genotyping was performed using the polymerase chain reaction and TaqI digestion. The e4 frequency was calculated by allele counting and the differences between groups tested with Fisher's exact test. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated with GraphPad InStat (1994) V2.05a software.

The table shows the genotypes and allele frequencies of each group. The e4 allele frequencies for late onset Alzheimer's disease patients and controls were 0.22 and 0.077 respectively. Homozygosity for the e4 allele was found in three patients in the Alzheimer's disease group and none among controls. Our young population had an e4 allele frequency of 0.153 which agrees with the reported frequencies for white populations. We found a statistically significant difference between patients with late onset Alzheimer's disease and controls (P = 0.015) but not between the Alzheimer's disease group and the young population (P = 0.26). The OR for our case control study, in the presence of one or two e4 alleles, was 3.33 (95% CI 1.204-9.020). Although our results are in general agreement with most reports, we found a rela-
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