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Effect of cannabinoids on spasticity and ataxia in multiple sclerosis*

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Summary. The chronic motor handicaps of a 30-year-old multiple sclerosis patient acutely improved while he smoked a marihuana cigarette. This effect was quantitatively assessed by means of clinical rating, electromyographic investigation of the leg flexor reflexes and electromagnetic recording of the hand action tremor. It is concluded that cannabinoids may have powerful beneficial effects on both spasticity and ataxia that warrant further evaluation.

Key words: Multiple sclerosis – Spasticity – Ataxia – Cannabinoids – Flexor reflex

Introduction

This study was prompted by a young man with multiple sclerosis (MS) who used marihuana as a remedy for his various motor, micturition and sexual handicaps. After smoking a marihuana cigarette on the ward, he clinically improved. He agreed to the beneficial effects of marihuana being investigated by means of quantitative clinical and electrophysiological assessment.

Case report

This male patient, born in 1955, had had MS since 1983. At the time of our experiments he was bound to a wheelchair because of severe limb and gait ataxia and spastic tetraparesis. After micturition, his residual urine volume was 100–150 ml. He complained of impotence, with erections lasting less than 5 min and lacking ejaculation. He tried a marihuana cigarette in about 1984 and noted an instantaneous improvement of his motor and sexual functions lasting for several days. Since then, he regularly took some marihuana biscuits each week, which enabled him to climb stairs, to walk on even ground, and to have erections for more than 30 min, allowing him a quite satisfactory sexual life.

Methods

From 12 October 1985 the patient abstained from all drugs, including marihuana. He was hospitalized between 17 October and 25 October. On 22 October, one "experimental" marihuana cigarette was allowed, and various electrophysiological experiments were performed as described below.

Clinical rating was performed daily by the same neurologist and on 22 October before and after the "experimental" cigarette. Rating comprised motor functions relevant to the electrophysiological tests described below (see Fig. 1).

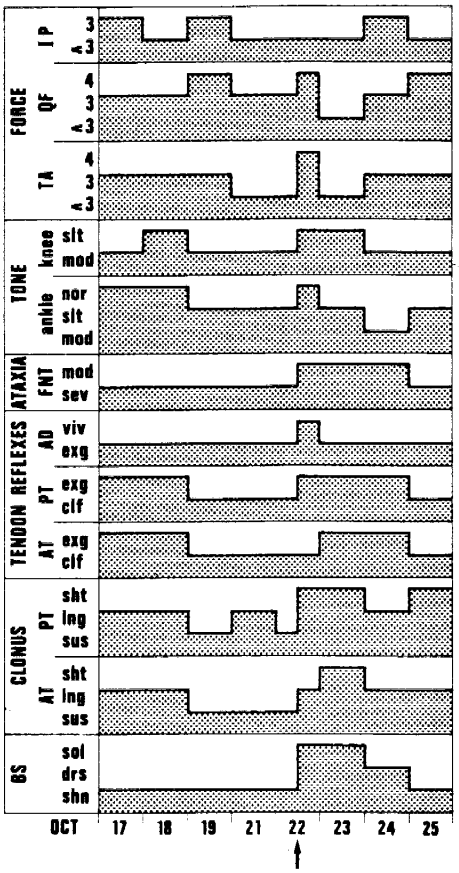

Fig. 1. Results of clinical rating *(shaded)* on the days before and after smoking the marihuana cigarette (*arrow* on time scale). Force (according to the MRC scale) of the iliopsoas *(IP)*, quadriceps *(QF)*, and tibialis anterior *(TA)* muscles. Muscle tone (knee and ankle joints): normal *(nor)*, slightly *(slt)* and moderately *(mod)* increased. Ataxia at finger-nose testing *(FNT)*: moderate *(mod)*, severe *(sev)*. Deep tendon reflexes of the achilles *(AT)* and patella tendons *(PT)* and hip adductors *(AD)*: very brisk *(viv)*, exaggerated *(exg)*, cloniform *(clf)*. Ankle *(AT)* and patella *(PT)* clonus: short *(sht)*, long *(lng)*, sustained *(sus)*. Babinski sign *(BS)* elicitable from the foot sole *(sol)*, foot dorsum *(drs)*, shin *(shn)*

* Dedicated to Professor H. H. Kornhuber on the occasion of his 60th birthday

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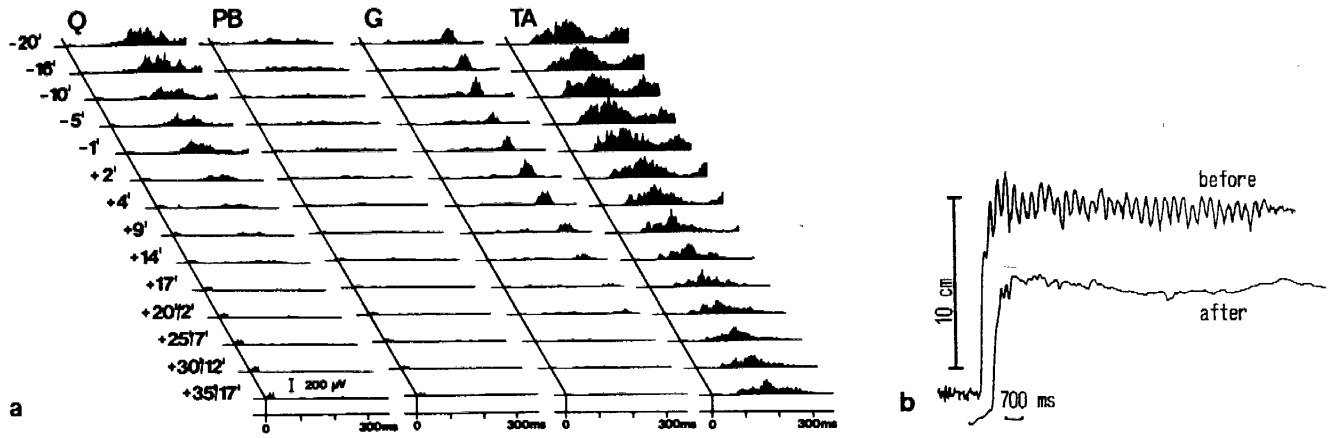

Fig. 2a, b. Influence of smoking two whiffs of a marihuana cigarette on **a** the abnormal flexor reflex, and **b** on the finger and hand action tremor. **a** EMG records from the quadriceps *(Q)*, posterior biceps *(PB)*, gastrocnemius *(G)* and tibialis anterior *(TA)* muscles. Each recording represents eight rectified and summated reflexes. Figures to the left indicate the time before (−) and after (+) the first whiff, the second whiff being taken 18 min after the first. Vertical and horizontal calibrations apply for all recordings; stimulation at 0 ms. **b** Electromagnetic recording of the finger and hand action tremor in a pointing task on the morning before and in the evening after smoking the marihuana cigarette

The *flexor reflex* was elicited by a painful electrical shock to the foot sole and recorded from the quadriceps (Q), posterior biceps (PB), gastrocnemius (G) and tibialis anterior (TA) muscles. The EMG was full-wave rectified, and eight consecutive reflexes were summated. Five control series of eight consecutive reflexes each were run at intervals of about 5 min. The patient was then asked to take one whiff of his "experimental" cigarette, and further series of reflexes were run in the manner described above (for details see [12]).

Finger movements were recorded in a standardized pointing task performed before and after both the "experimental" cigarette and the flexor reflex experiment. Basically, the recording device consisted of a three-coil-transmitter system generating non-homogeneous magnetic fields, and a miniaturized receiver coil attached to the finger tip. When the finger moved through the magnetic fields a signal was induced in the receiver coil, allowing the computation of the two-dimensional movement trajectory (for details see [15]). Ten trials were performed before and after marihuana smoking, each consisting of a pointing movement of the right index finger over a 10-cm distance. The forearm rested on a stable support, but the finger and hand could not reach the target.

Results

Clinical rating showed a moderate deterioration of motor functions between 17 October and 22 October (Fig. 1). On 22 October, before the "experimental" cigarette, he was incapable of walking a few steps even with support; his muscle force in the legs did not exceed MRC grade 3. Muscle tone ranged between slightly and moderately increased, and the leg deep tendon reflexes were exaggerated or clonic with sustained ankle and knee clonus. The receptive field of the Babinski sign covered the whole foot and the shin. Ataxia in the arms was severe and could not be tested in the legs because of distinct hip flexor paresis.

About 45 min after the marihuana cigarette, muscle force was somewhat increased in the knee extensors and ankle flexors (but not in the hip flexors), and muscle tone was reduced. The leg deep tendon reflexes showed normalization, too, corresponding to a clear shortening of the periods of clonus. The receptive field of the Babinski sign was confined to the lateral foot sole margin. Ataxia in finger-nose testing was moderate. After the flexor reflex experiment, the patient was able to walk a few metres between the couch and his wheelchair with support. Some of these improvements lasted beyond 23 October and even 24 October (Fig. 1).

The flexor reflex showed the desynchronized and prolonged reflex pattern typical of spastic paresis (Fig. 2a; cf [13]). As soon as 2 min after the whiff of the marihuana cigarette, a clear attenuation of the reflex activity was noted. Attenuation was about equal in all four muscles (20%–30% of the last three control recordings) and progressed until 17 min after the whiff. A second whiff (18 min after the first one) did not induce further reflex attenuation. Single sweep recordings showed that the reflex attenuation after marihuana was not due to enhanced habituation: after marihuana even the first of the eight consecutive reflex responses was attenuated.

Electromagnetic recording of action tremor revealed a coarse 3 Hz hand and finger tremor with an amplitude between 1 and 3 cm, persisting throughout nearly the whole movement. Hours after the "experimental" cigarette, action tremor was almost completely abolished, although the movements were made at about the same speed (Fig. 2b).

Discussion

Our findings clearly show that there are indeed motor actions of marihuana which were (a) reproducible in a laboratory situation most exhaustive to the patient, (b) quantitatively assessable by means of electrophysiological testing, and (c) in line with the results of clinical rating. Our findings further correspond with earlier anecdotal clinical reports [4, 6, 11, 14].

Little is known about the neurophysiological background of the antispastic and antiataxic actions of marihuana seen in our patient. However, some findings in experimental animals seem relevant to our observations. Cannabinoids in higher

dosages attenuate the monosynaptic reflex [1, 2, 17, 18] principally corresponding to the attenuation of both deep tendon reflexes and clonus in our patient (Fig. 1). Polysynaptic reflexes were also attenuated after tetrahydrocannabinol derivatives in experimental animals [1, 7, 20], fitting in well with the narrowing of the receptive field of the Babinski sign (Fig. 1) and with the results of our flexor reflex experiment. As cannabinoids have analgesic properties [16, 20], attenuation of the pathological flexor reflex in the present case could represent analgesic rather than antispastic effects of the drug. However, analgesic effects are also attributed to several antispastic drugs [10, 21] and, on the other hand, classical analgesics such as opioids may improve spastic symptoms [19]. One might, therefore, indeed wonder whether both the antispastic and analgesic actions of such drugs are in fact at least to a substantial degree based on common neuronal mechanisms such as an increase of presynaptic inhibition or a decrease of postsynaptic excitation of multireceptive interneurones at various levels of the neuraxis. Whatever the mechanism, the antispastic actions of marihuana in both clinical rating and electrophysiological testing are similar to those seen in spastic patients after either 0.3 mg tizanidine [13], 150 µg clonidine, or 10 mg diazepam (unpublished observations). The important difference is that marihuana apparently also has antiataxic actions (Fig. 2b; see also [4]) not ascribed to any antispastic drug.

The biochemical basis of the motor effects of marihuana is obscure. Available data, although somewhat controversial, suggest that cannabinoids release brain serotonin from its storage sites and block its re-uptake [8], inhibit the synthesis of prostaglandins within the CNS [9] and – in large doses – elevate brain acetylcholine and reduce its utilization [5]. The relationship of these neurotransmitters to spasticity and ataxia is unknown: none of the well-established antispastic drugs is thought to interfere with them; they are only scarcely, if at all, found within the cerebellum [3].

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