Continuous involuntary hand movements and schizencephaly: epilepsia partialis continua or dystonia?

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Abstract

Schizencephaly is regarded as a malformation of cortical development (due to abnormal neuronal organization) and may be associated with continuous involuntary hand movements. The mechanisms underlying these movements are not clear and both dystonia and epilepsia partialis continua have been considered in previously reported cases. We describe a young patient affected by schizencephaly and continuous involuntary movements of the contralateral hand. Functional MRI showed bilateral cerebral activation while the subject performed tapping movements with the affected hand and no significant difference in the activation pattern after diazepam infusion. Standard and back-averaged EEG showed no alterations. The results obtained from these investigations and the clinical features of the involuntary movements are not in favour of an epileptic genesis, while support the diagnosis of secondary dystonia.

Keywords: Dystonia, Epilepsia Partialis Continua, Functional MRI, Involuntary Movements, Schizencephaly

Introduction

Schizencephaly is defined as a malformation of cortical development due to abnormal neuronal organization. It refers to a cleft extending from the cerebral cortex to the ventricle, can be unilateral or bilateral and tends to involve the insular, precentral and postcentral regions. Schizencephaly is classified as type 1 or “closed lip”, when referring to clefts which are closed, and type 2 or “open lip”, where larger defects are extended to the ventricle[1]. While type 1 defects are usually associated with minor deficits such as a mild hemiparesis and partial seizures, type 2 may be associated with developmental delay, microcephaly, seizures and spasticity[1]. Schizencephaly may be associated with movement disorders, but underlying physiopathologic mechanisms are unclear. Two cases have been published describing patients with permanent focal continuous involuntary movements of the hand. The first patient was diagnosed as delayed-onset dystonia[2], while the second as epilepsia partialis continua (EPC)[3]. We describe a patient with clinical features very similar to these previous cases, discussing the diagnostic findings and the physiopathologic hypothesis.

Case report

A 32-year-old right-handed woman presented involuntary left hand fingers movements since she was a child. The movements consisted in continuous flexion, adduction and abduction movements of the second and third finger at about 1Hz frequency (see video). Although polysomnographic study have not been performed, patients' relatives reported that the involuntary movements disappeared during sleep. The patient reported no injuries during birth and no alterations in psychomotor development; no cognitive deficits were present. The patient had been diagnosed with polycystic ovary syndrome, migraine without aura and a left Bell palsy which recovered completely. No seizure history has been reported. The neurological examination disclosed no additional involuntary movements in other segments, no signs of hemiparesis, spasticity or other neurological deficits, although the voluntary movements performed with the left hand were clumsy and precision finger grip was impaired. Mirror movements could be detected in the right hand while the patient was performing finger tapping movements with the affected hand.

The patient underwent a brain MRI scan that disclosed an open-lip schizencephaly involving right posterior frontal cerebral cortex (Figure 1). Standard and back-averaged EEG were normal, as well as somatosensory evoked potentials to median nerve stimulation. A functional MRI (fMRI) study was performed at rest and during a motor task with either hands, before and after intravenous diazepam 10mg infusion (Figure 2). The motor task consisted in tapping the thumb with the other four fingers, one at a time, following a metronome pacing tones at 1Hz frequency (note that the metronome played also during the rest condition). Before diazepam, a task versus rest contrast during motor performance with the right unaffected hand indicated increased activation of the left cerebral hemisphere involving primary motor cortex (BA4) and posterior frontal lobe, just anterior to the primary motor cortex (BA6), associative cortical areas of the inferior parietal lobe (BA40), primary somatosensory cortex (BA3), associative areas (BA22) and primary auditory cortex (BA41). A task versus rest contrast during motor performance with the left affected hand, showed a wider cerebral activation, involving the same areas cited above, but bilaterally.

After diazepam infusion, the involuntary left hand movements were reduced and disappeared for a few seconds, while the patient was asleep. The functional MRI scan performed after the infusion showed the same pattern of activation, with no significant difference in intensity compared to the baseline condition.

Discussion

Schizencephaly associated with permanent focal continuous involuntary movements of the hand has been described in only two previously published cases. The first patient was described by Friedman et al in 1996 as a case of delayed-onset dystonia[2]. The second one was reported by Zyss et al in 2007 and considered affected by EPC[3]. While the patient by Friedman presented a pattern of slow dystonic movements with a nearly fixed hand posture, the patient described by Zyss showed faster repetitive finger movements, very similar the our case. The involuntary movements observed in our patient and the one by Zyss are consistent with athetosis, however recently the distinction between athetosis and dystonia was tempered, with athetosis being considered a further subtype of dystonic movement [4]. Moreover, athetosis is frequently observed in the setting of a life-long, static encephalopathy [5]. Given such a striking similar movement pattern and cortical malformation between our patient and the one described by Zyss, a similar physiopathologic process might be suggested.

Epilepsia partialis continua and secondary dystonia are both conditions that may explain a pattern of continuous involuntary movements of the hand. Disease history, clinical information and specific investigations may provide elements to foster either EPC or dystonia as the process underlying the continuous involuntary movements in schizencephaly.

Epileptic seizure may often appear during sleep and involuntary movements related to EPC have been reported to persist in about 50% of patients[6]. Sleep usually suppresses the involuntary movements related to different extrapyramidal disorders, including dystonia[7]. The involuntary movements persisted during sleep in the patient described by Zyss, while were greatly reduced or absent in our patient.

The presence of heterotopic cortex increases the risk of epilepsia[8] and cortical dysplasia has been associated with EPC[9]. The case by Zyss has been reported having polymicrogyria and heterotopia along with the schizencephalic lesion, which can of course be considered an element in favour of the diagnosis of EPC. It must be noted that the presence of "abnormal cortex" at cleft vertex was reported in the case of delayed-onset dystonia reported by Friedman. The MRI scan in our patient did not show the presence of heterotopic cortex or cortical dysplasia. It could be interesting to note that both the previous cases were affected by a preexisting mild hemiparesis involving the same side where the involuntary movements were present.

While moving the affected hand, bilateral cortex activation was present in both our and the patient described by Zyss. In the former, the authors discussed such pattern of activation as due to "abnormal brain plasticity seen in dystonia", curiously supporting the hypothesis of a dystonic pathogenesis and not of an epileptic mechanism. Our patient presented mirror movements in the right hand while performing finger tapping movements with the affected hand. This could account for the bilateral brain activation that was observed during fMRI. Such bilateral activation pattern has been also found in patients with writer cramp and mirror movements[10] and probably reflects impaired transcallosal inhibition from the right affected to the left unaffected cortex, while the activation of ipsilateral motor pathways is more unlikely since the cortical activation while moving the unaffected hand was strictly contralateral.

After diazepam infusion, Zyss reported an increased activation of the malformed cortex during the motor task compared with the rest condition. This has been explained hypothesizing that diazepam had decreased the cortical activity during rest, determining a task versus rest significant difference. Our patient performed a similar experimental protocol during the fMRI investigation and no difference could be found comparing the scans before and after diazepam infusion, both at rest and during the motor task. Such data support the absence of a substantial effect of the drug on the neuronal

activity sustaining the involuntary movements.

The presence of an epileptic focus recordable over the brain cortex would confirm the diagnosis of EPC, anyway it has been reported that only about 22% of the patients with EPC had EEG epileptic abnormalities, even if the sensitivity in detecting epileptic spikes can be increased using a jerk-locked back-averaging technique[6]. Both our and Zyss patient performed EEG recordings which disclosed no abnormalities. Our patient performed also a back-averaged EEG which detected no potentials.

According to Pandian[11] and Cockerell[6], in EPC the number of jerks per minute is usually less than 10. In both our and Zyss case the jerks occurrence is much higher than 10 per minute, as clearly shown by the video recordings.

Epilepsia partialis continua is difficult to treat and usually requires two or more antiepileptic drugs in order to control the seizures[12]. Medical treatment of dystonia is very difficult and there is no recommended evidence-based oral treatment. Though anticholinergic drugs and tetrabenazine might exert benefits in some patients, benzodiazepines may be used as an ancillary therapy than exploits the muscle relaxant properties[13]. Zyss reported a reduction of the involuntary movements after diazepam infusion and also benefit taking oral clobazam. Furthermore, a mild improvement following anticholinergic drug administration has been reported. Our patient showed a transient reduction of the involuntary movements after diazepam infusion, but no other treatments have been proposed since the involuntary movements did not interfere with daily activities.

Considering our patient, the clinical features of the involuntary movements, the lack of EEG and back-averaging alterations and the absence of diazepam effect on the brain activation pattern are in favour of a diagnosis of secondary dystonia. In our opinion, in patients with schizencephaly presenting with continuous involuntary movements of the contralateral hand, dystonia should be considered as the first diagnostic hypothesis, while EPC should be addressed only if a clear epileptic activity can be demonstrated.

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Figure 1

T2 axial scans showing a right posterior frontal sulcus reaching the lateral ventricle, compatible with an open-lip schizencephaly

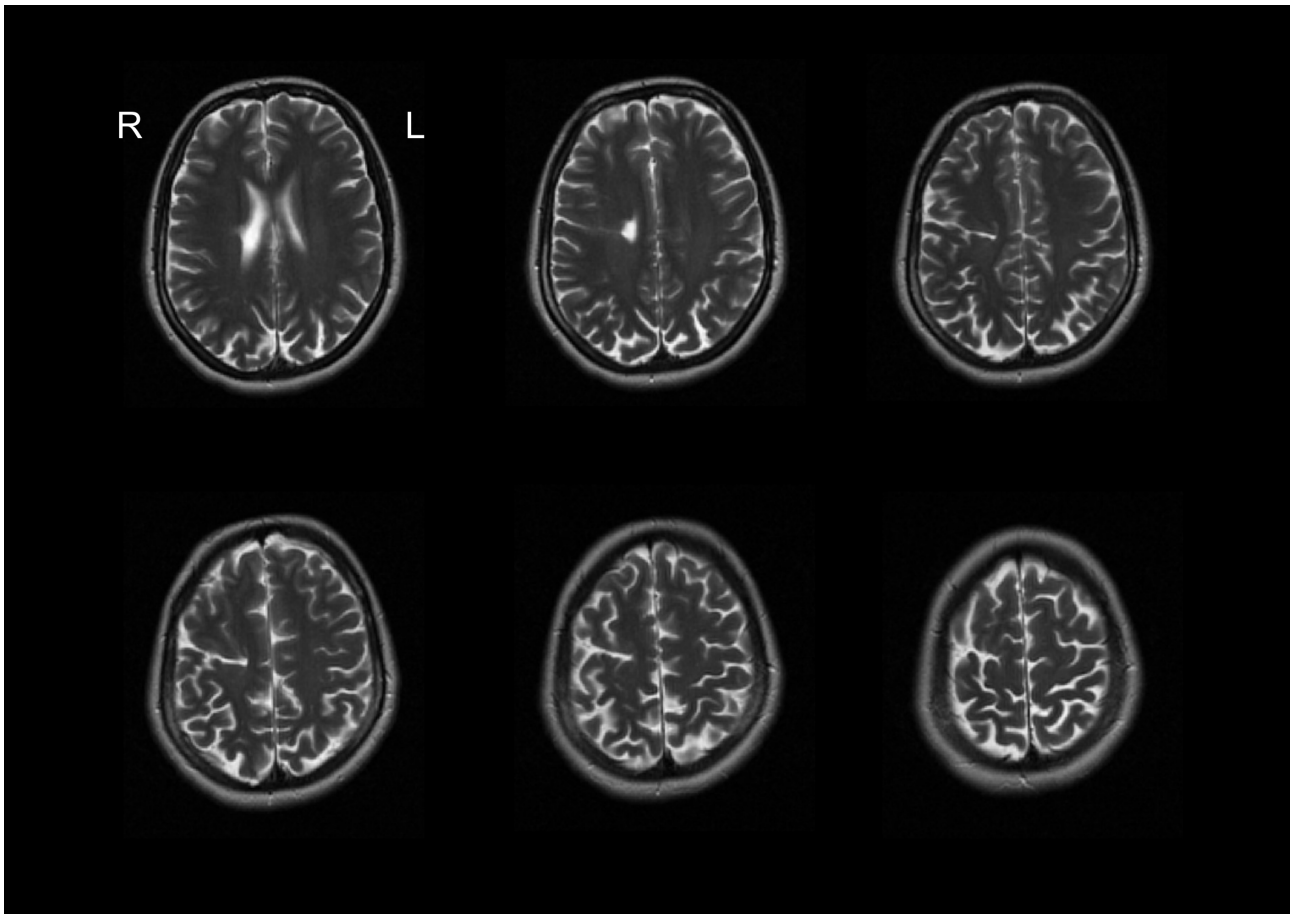

Figure 2

Brain activation maps obtained by the analysis of fMRI scans, showing bilateral brain activation during tapping with the left affected hand and no significant difference in the pattern and intensity of the activation after diazepam infusion