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Abstract

Pervasive developmental disorder is characterized by various symptoms that often include self-injurious behavior (SIB). Episodes of SIB occur in the context of high emotional arousal, anger, or fear and may be related to epilepsy. We report the case of a 20-year-old man with pervasive developmental disorder presenting with SIB non-responsive to antipsychotic medication. Positron emission tomography showed a right temporoparietal hypometabolic focal lesion suggestive of an epileptic focus. Two weeks after initiation of levetiracetam (Keppra®), SIB disappeared, without recurrence 24 months later. Levetiracetam (Keppra®) may be beneficial for such patients.

Reference


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Treatment with levetiracetam in a patient with pervasive developmental disorders, severe intellectual disability, self-injurious behavior, and seizures: A case report

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Pervasive developmental disorder is characterized by various symptoms that often include self-injurious behavior (SIB). Episodes of SIB occur in the context of high emotional arousal, anger, or fear and may be related to epilepsy. We report the case of a 20-year-old man with pervasive developmental disorder presenting with SIB non-responsive to antipsychotic medication. Positron emission tomography showed a right temporoparietal hypometabolic focal lesion suggestive of an epileptic focus. Two weeks after initiation of levetiracetam (Keppra®), SIB disappeared, without recurrence 24 months later. Levetiracetam (Keppra®) may be beneficial for such patients.

Keywords: PDD; ID; Seizure; Self injurious behavior; PET imaging; Levetiracetam.

Pervasive developmental disorders (PDD), otherwise known as autistic spectrum disorders, are characterized by severe and pervasive impairment in several areas of development, including reciprocal social interaction and communication skills, and the presence of stereotyped behavior, interests, and activities. The quantitative impairments that define these conditions are distinctly deviant relative to the individual’s developmental level or mental age (American Psychiatric Association, 1996). PDD constitute a life-long disabling condition and, except for Rett disorder, lack an exact etiological and neurobiological definition. Intellectual disability (ID), however, is common and varies in severity.

Epileptic seizures and epilepsy have frequently been reported in PDD, with an incidence of 4–42% (Giovanardi Rossi, Posar, & Parmeggiani, 2000). The occurrence of epilepsy in autistic persons is higher than that in the general population (Danielsson, Gillberg, Billstedt, Gillberg, & Olsson, 2005). Several reports have suggested that autistic individuals are at a greater risk for developing seizure disorders, particularly in adolescence. Olsson, Steffenburg, and Gillberg (1988) reported that in a population of children under the age of 10 years with autism, epilepsy was found in 20% of the cases; all types of epilepsy were seen. Other studies (Volkmar & Nelson, 1990) reported that in a series of 192 autistic individuals, 21% of cases had exhibited a seizure disorder and that age-specific incidence revealed a 3–22-fold increase in risk for seizures relative to the normal population.

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Episodes of aggressive behavior (aggression toward others or property) related to epilepsy have gained considerable attention because they represent an important social and clinical problem (Marsh & Krauss, 2000; Schachter, 2001). Three different types of aggressive behaviors have been distinguished on the basis of their relation to the seizure event: (i) interictal, (ii) ictal, or (iii) postictal aggression (Delgado-Escueta et al., 1981). Anatomic and electrophysiological data suggest that a temporal and frontal dysfunction occurs in ictal/post-ictal biting behavior and that all these aggressions occur in the context of high emotional arousal, anger, or fear (Marsh & Krauss, 2000; Tassinari et al., 2005). Studies have reported self-injurious behavior (SIB), including bruising of the limbs and biting of the tongue and lips (Peguero, Abou-Khalil, Fakhoury, & Mathew, 1995), associated with psychogenic seizure. No studies have reported biting of hands and arms in patients with PDD and severe ID associated with epilepsy or psychogenic epilepsy.

In our patient with PDD and severe ID, epilepsy could have mimicked behavior disorders as SIB with biting behavior (hands and arms). Electroencephalography was inconclusive; therefore, FDG PET findings were central to discovering the possible epileptic origin of the behavior. This would permit the introduction of adequate treatment with levetiracetam (Keppra®) and reduction of the antipsychotic treatment.

**CASE REPORT**

A 20-year-old man with PDD and severe ID was hospitalized for episodes of hyperactivity and SIB non-responsive to several psychotropics among which antipsychotics. This patient was treated successively with pipamperone (40 mg/day), levomepromazine (125 mg/day), olanzapine (15 mg/day), zuclopenthixol depot (100 mg/15 days), haldol (5 mg/day), and promazine (100 mg/day). He also received the antidepressant venlafaxine (18.75 mg/day) and benzodiazepine as clonazepam (3 mg/day). The different treatments obtained very poor results.

Clinical evaluation showed recurrent episodes of severe SIB, such as biting of hands and arms, occurring only at the end of the afternoon between 17:00 and 19:00 h and lasting from 20 minutes to a maximum of 2 hours. We noticed that immediately before these episodes, he experienced listening attitude, probable hallucinations, agitation (expressed as running with large strides through the corridors), and repetitive striking with the toilet brush onto the WC seat. These phases of psychomotor seizure were followed by a clastic crisis with loss of contact, cries, and mutilations in the form of deep bites in the hands and arms that we can consider as postictal aggression.

The presence of repetitive gestures (percussions) during the ‘aura’, the timing (evening), the duration of the crisis, and the loss of contact during the crisis were suggestive of epileptic disorder.

Electroencephalography was inconclusive and it presented a basic bilateral and symmetrical alpha rhythm of 8–9 Hz. Compliance during the investigations was absent, and the patient was sedated with antipsychotics. Indeed, it was not possible to perform electroencephalography during the episodes of severe automutilation.

The patient underwent cerebral imaging with PET imaging with F-18 2-fluoro-2-deoxyglucose (F-18 FDG) and MRI for further investigation. The patient was administered general anesthesia because of the absence of compliance. FDG PET showed a focal hypometabolic lesion in the right temporoparietal region that was highly suggestive for an epileptic focus, whereas MRI showed no pathology in this location. In addition, PET was consistent with diffusely decreased metabolism in the posterior fossa due to a cystic lesion, in concordance with MRI findings. No sign of acute hydrocephalus was found.

Figure 1a shows the transaxial view of PET with focal diminution of the FDG uptake in the right temporoparietal region. MRI shows no abnormality in this region (Figure 1b).

Figure 2a shows the transaxial view of PET with diffuse diminution of FDG uptake in the left posterior fossa. The cyst in the temporoparietal region in MRI in Figure 2b is superposable to this hypometabolism.

FDG PET was performed for an epileptic workup in order to find a functional correlate to epileptic crises. FDG PET imaging showed a single hypometabolic focus in the temporoparietal region consistent with an epileptic focus.

Hypometabolism located at the temporal level is not exclusively indicative of temporal epilepsy. However, in the case of a young adult and in the absence of signs or symptoms of degenerative
disorder, this type of metabolism can be correlated to a comitiality, especially considering that comitiality is present in almost 50% of people with autism.

Treatment with anti-epileptic medication, levetiracetam (Keppra®; 2 g/day), was initiated, and 2 weeks later, the SIB disappeared with no recurrence 2 years later.

We chose treatment with levetiracetam (Keppra®) because of the possible double action on epilepsy and on non-epileptic symptoms such as stress, anxiety, and panic; this action has been reported, even if not definitively assessed, by some authors (Farooq et al., 2009; Rugino & Samsock, 2002; Mattes, 2008; Wasserman et al., 2006).

Figure 1. (a) Transaxial view of PET showing focal diminution of the FDG uptake in the right temporoparietal cortex. (b) MRI shows no abnormality in this region.

Figure 2. (a) Transaxial view of PET shows diffuse diminution of FDG uptake in the left posterior fossa. (b) MRI shows a cystic lesion in this region.
The presence of SIB, particularly biting behavior with lesions to hands and arms, is extremely distressing for patients, families, and professionals. In the literature, there is no description of biting hands and arms in patients with PDD and severe ID mimicking epilepsy or psychogenic epilepsy. SIB with bruising of the limbs and biting of the tongue and finger in Lesch–Nyhan syndrome has been reported in the literature. Biting of the inferior lip and finger in Lesch–Nyhan syndrome has been reported (McManaman & Tam, 1999) without a diagnosis of epilepsy.

Tassinari et al. (2005) described biting behavior in epilepsy, but not self-biting behavior. Other authors have described non-epileptic seizures with paroxysmal episodes of motor, sensory, and emotional signs but without self-biting behavior (Hubsch et al., epub in press; Reuber & Duncan, epub in press).

In patients with PDD and severe ID it is almost impossible to obtain a technically acceptable EEG, and the behavior disorders are so important and dangerous for physical integrity that a psychoactive medication has to be used. In neurology, PET imaging using FDG is being used in a broad spectrum of clinical indications, including tumor, neurodegenerative and vascular disorders, and epilepsy. FDG PET imaging procedures have been described in the investigation of epilepsy and are being used as a complement imaging device to MRI (Chugani, 1994).

There are scarce data in the literature describing FDG-PET for imaging PDD patients presenting with epilepsy mimicking auto-aggressive behavior disorders. Considering the higher risk of PDD patients developing epileptic crises (Bouilleret et al., 2005; Giovannardi Rossi, Parmeggiani, Bach, Santucci, & Visconti, 1995), imaging with FDG PET represents a method of high sensitivity for detection of focal cerebral metabolic abnormalities highly suggestive for epileptic foci, even in patients without major anatomical cerebral abnormalities that would explain focal disease (Schifter et al., 1994).

In PDD patients with epilepsy, the diagnosis of the focal lesion is essential for an effective treatment. In these patients, clinical diagnosis of epilepsy becomes extremely difficult; therefore, complementary investigation by means of modern imaging techniques is of great importance for the identification of the focal lesion.

It is important to stress that the patients who have problems with compliance could present a level of agitation that prevents recording of an EEG under acceptable technical conditions and that with the necessary sedation, the EEG may not be conclusive. PET scan under general anesthesia can provide information important to diagnosis and treatment that may be otherwise unobtainable.

Anti-epileptic treatment can be reasonably initiated only after adequate identification of the focal lesion suggestive of an epileptic focus. Non-invasive imaging techniques, such as CT, MRI, and PET allow visualization of cerebral abnormalities in PDD patients (Davidson, Thomas, & Casey, 2003; Eigisti & Shapiro, 2003; Kennedy, Haselgrove, & McInternery, 2003). MRI can be used to visualize cerebral structures, including basal ganglia, defects of myelinization, and subtle abnormalities such as cortico-cerebellar dysplasia (Soto-Ares, Joyes, Lemaître, Vallée, & Pruvo, 2003) and abnormalities of the septum pellucidum (Kennedy et al., 2003).

Although anatomical abnormalities have been described in autistic patients by MRI (Miles et al., 2005), their functional impact is not clear. Interestingly, MRI may be normal or show only subtle abnormalities in patients with temporal epilepsy who show significant focal hypometabolism in FDG PET. The contribution of MRI in imaging epilepsy is characterized by its high sensitivity; however, nuclear medicine imaging techniques including SPECT and FDG PET show higher sensitivity and specificity (Spencer, 1994).

The treatment with levetiracetam (Keppra®), because of the possible action both on epilepsy and on stress, anxiety, and panic, could be an interesting pharmacological approach for patients with PDD, severe ID, and SIB presenting a focal lesion suggestive of an epileptic focus.

FDG PET has been used to characterize cerebral metabolism in different groups of PDD patients (Happe et al., 1996) and under different conditions, such as resting (George, Costa, Kouris, Ring, & Ell, 1992; Hashimoto et al., 2000; Ohnishi et al., 2000), sleeping (Zilbovicius et al., 1995), and while under stress (Buchsbaum et al., 1992; Muller et al., 1998; Siegel et al., 1992; Siegel, Nuechterlein, Abel, Wu, & Buchsbaum, 1995). Most studies agree that the benefits of imaging are greater than the risks of anesthesia required in this group of patients (Curry et al., 1997).
CONCLUSION

FDG PET may contribute essential metabolic information for the localization of possible epileptic foci in patients with PDD, severe ID, and SIB, allowing more precise diagnoses and treatment adjustments. The use of levetiracetam (Keppra®) could be considered as an interesting approach to control SIB in these patients. In addition, FDG PET might be of particular interest to monitor disease evolution under treatment.

REFERENCES


