

## EDITORIAL

# Artificial Intelligence and Pediatric Neurology

## Inteligência Artificial e Neurologia Pediátrica

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The ultra-fast development of artificial intelligence (AI), and the immensity of hope and fear it generates, is fascinating. To illustrate the announced revolution related to the most recent advances in the domain, UNO's Secretary General António Guterres published a warning statement highlighting the need for urgent regulation of AI tools and put specific emphasis on its use in the military domain. Similarly, in a common tribune, the creators of some of the most recent AI tools themselves raised concerns about their future development and use.

On a more modest level, that of our humble clinical environment, it is long acquired that AI will help assisting numerous important diagnosis and patient management procedures. To name a few, these include large-scale data analysis and comparison for early imaging diagnosis and prognosis, medical summary writing based on data extraction from patient electronic files, and long-term EEG seizure or spike detection, for example.

Similarly, many researchers have already integrated the use of various forms of AI in their academic activities. These include writing summaries of available knowledge on a specific field, text editing, graphic presentation of large datasets, or generation of research projects ideas, among many more. Concrete results may emerge in clinical practice very soon. Interesting research projects use AI platforms in the aim of repurposing existing drugs to better treat certain rare diseases due to specific gene variants, for example.

As a consequence, many hospitals and academic institutions have started to propose teaching sessions dedicated to AI-related challenges in their medical study program (while nevertheless highlighting the need for strict and continuously updated usage regulations).

One interesting question that arises is how patients themselves will interact with conversational robots (chatboxes), and how this usage will affect their medical care and their relationship with caregivers. Will patients and families be able to understand and reprocess the information given by chatboxes without our additional explanations, without our personal advice and sympathy...? The question is open...

As impressive as is the generation in just a few seconds of a 500-word answer to a quite complex question, we all need to remember that the mechanism used by chatboxes to generate these paragraphs is far from being «intelligent» in the sense we usually understand it for human beings... Chatboxes «just» propose average sequences of words grouped according to their frequency of association in the sources used. Major weaknesses of this «statistical» approach include the lack of ponderation of the information found, and the absence of source citation, that may prevent correct interpretation and replacement in the personal context of a given patient by non-experts.

To illustrate these limits, here are 3 examples of answers to medical questions given by the ChatGPT free testing system called Playground (<https://platform.openai.com/>, version GPT-3.5-turbo-16k, answer voluntarily limited to 500 words by the author of the questions). These are followed by personal comments.

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**Q1: How do you treat absence seizures?**

«Absence seizures, also known as petit mal seizures, are a type of generalized epilepsy seizure characterized by brief episodes of impaired consciousness without convulsions or major motor symptoms. Here are some common treatment approaches for absence seizures:

1. Antiepileptic medications: The first-line treatment for absence seizures is typically antiepileptic medications. The most commonly prescribed medications include ethosuximide, valproic acid, and lamotrigine. These medications help regulate abnormal electrical activity in the brain, reducing or eliminating absence seizures. The choice of medication will depend on factors such as the individual's age, coexisting medical conditions, and potential side effects.

2. Lifestyle modifications: Certain lifestyle modifications can help manage absence seizures. Good sleep hygiene, regular sleep patterns, and adequate sleep duration are important as sleep deprivation can trigger seizures. Stress reduction techniques, including relaxation exercises and mindfulness, may also be helpful in some cases.

3. Ketogenic diet: In some cases, a ketogenic diet may be considered for the treatment of absence seizures. This high-fat, low-carbohydrate diet has been shown to be effective in reducing seizure activity in some individuals with epilepsy, including absence seizures. It is typically implemented under the guidance of a registered dietitian or medical professional experienced in ketogenic diets.

4. Vagus nerve stimulation (VNS) therapy: VNS therapy involves implanting a small device that stimulates the vagus nerve in the neck. It is an adjunctive treatment option that may be considered for individuals with drug-resistant absence seizures who are not eligible for surgery. VNS therapy has shown to reduce seizure frequency in some patients.

5. Other therapies: In cases where medication and other conventional treatments do not effectively control absence seizures, other interventions like responsive neurostimulation (RNS) or epilepsy surgery may be considered. However, these options are typically reserved for individuals with drug-resistant seizures and require evaluation and discussion with an epilepsy specialist.»

*Personal comment: Although this answer includes some relevant points, lots of important aspects are lacking. The definition of absences is quite vague, there is no mention of their specific EEG correlate, the typical age of onset is not*

*specified, The ILAE classification proposal and its subcategories of absences is not cited. Most sentences are very general, others do not apply at all to typical absences («epilepsy surgery may be considered... »!).*

**Q2: Which investigations are indicated in a 3-year-old girl with absence seizures?**

«In a 3-year-old girl with absence seizures, a comprehensive evaluation would typically involve several investigations to diagnose and understand the underlying cause of the seizures. Here are some commonly indicated investigations:

1. Electroencephalogram (EEG): An EEG is essential for the diagnosis and classification of absence seizures. It helps record and analyze the brain's electrical activity, allowing for the identification of characteristic patterns associated with absence seizures, such as generalized 3 Hz spike-and-wave discharges.

2. Medical history and physical examination: A detailed medical history helps capture the frequency, duration, and characteristics of the absence seizures. A thorough physical examination is necessary to check for any neurological abnormalities or other signs that might be associated with the seizures or underlying conditions.

3. Genetic testing: Genetic testing may be recommended to identify any specific gene mutations or genetic abnormalities associated with absence seizures or related epilepsy syndromes. This investigation can help determine if there are any specific genetic factors influencing the seizures and guide treatment decisions or family counseling.

4. Blood tests: Routine blood tests may be conducted to assess general health, rule out any metabolic or electrolyte imbalances, and identify any underlying conditions associated with seizures. These blood tests may include a complete blood count, metabolic panels, liver and kidney function tests, and screening for genetic or metabolic disorders.

5. Imaging studies: While imaging studies are not typically considered for the routine evaluation of absence seizures, there may be certain cases where they are deemed necessary. Imaging studies, such as a brain MRI or CT scan, may be recommended if there are specific concerns about structural abnormalities or brain lesions that could be contributing to the seizures.

It is crucial to consult with a pediatric neurologist or epileptologist who specializes in evaluating and managing

ing seizures in children. They can guide the appropriate investigations based on the individual case and provide personalized care for the child with absence seizures. »

*Comment: The order in which these various points are given should be slightly different. Patient history and examination come always first! The EEG paragraph is correct, but no mention is made of the easy way to trigger absence seizures with hyperventilation. Bullet points 3-5 are too general to be useful. Most importantly, no mention is made of the early-age of onset (<4 years) of absences in this specific patient, which could suggest the need of a lumbar puncture to search for a GLUT1-deficiency syndrome, which is potentially treatable with a ketogenic diet...*

### **Q3a: Is valproic acid indicated in juvenile myoclonic epilepsy?**

«Yes, valproic acid (VPA) is commonly indicated and considered a first-line treatment option for juvenile myoclonic epilepsy (JME). JME is a specific epilepsy syndrome characterized by the presence of myoclonic jerks, generalized tonic-clonic seizures (*grand mal* seizures), and absence seizures.

Valproic acid has been shown to be effective in controlling the different seizure types associated with JME, including myoclonic jerks and generalized seizures. It works by stabilizing neuronal activity and inhibiting the spread of abnormal electrical discharges in the brain.

### **Q3b: Is valproic acid indicated in a 15-year-old girl with juvenile myoclonic epilepsy?**

«Yes, valproic acid (VPA) is commonly indicated in the treatment of juvenile myoclonic epilepsy (JME) in adolescents, including a 15-year-old girl. Valproic acid is considered a first-line treatment choice for JME due to its effectiveness in controlling different seizure types associated with the syndrome, including myoclonic jerks, generalized tonic-clonic seizures, and absence seizures. Considering the age of the patient, valproic acid is often a preferred option as it has a broad spectrum of action and can effectively target and control the various seizure types seen in JME. It is important to have a discussion with a pediatric neurologist or epilepsy specialist, as they can assess the individual's specific characteristics, medical history, and potential side effects of the medication.»

### **Q3c: How about teratogenicity?**

«Valproic acid (VPA) is known to have a higher risk

of teratogenicity compared to many other antiepileptic drugs. Teratogenicity refers to the potential to cause congenital malformations or developmental issues in the fetus if taken during pregnancy. Exposure to valproic acid during pregnancy has been associated with an increased risk of major congenital malformations, such as neural tube defects (e.g., *spina bifida*), craniofacial abnormalities, heart defects, and developmental delays. The risk appears to be dose-dependent, with higher doses associated with a higher risk of teratogenic effects. Due to this higher risk of teratogenicity, it is important to carefully consider the risks and benefits of using valproic acid in women of childbearing age, including 15-year-old girls, especially if there is a possibility of pregnancy. This decision should be made in consultation with a neurologist or epileptologist who specializes in epilepsy management, taking into account factors such as the individual's seizure control, overall health, and the availability of alternative treatment options. If valproic acid is deemed necessary, it is crucial to use effective contraception methods to prevent pregnancy while taking the medication. However, if the patient is already pregnant or planning to become pregnant, alternative treatment options with lower teratogenic potential may be preferred, and a thorough discussion should take place with healthcare providers to ensure the safest course of action for both the patient and the potential fetus.

Ultimately, the decision regarding the use of valproic acid should be based on an individualized assessment of the risks and benefits in each specific case, with careful consideration of the potential teratogenic effects and the patient's reproductive plans. »

*Comment: This interesting «dialogue» illustrates the importance of the formulation of the question. Patients unaware of the potential teratogenic effects of valproate are at risk of staying ignorant of this crucial point if they're satisfied with the answer to Q3a...*

Incomplete information, simplistic and general statements, errors... Although of definite interest, chatboxes will need to be improved to be really useful in our clinical practice. Google research is currently developing a new tool called Med-PALM 2. This tool, designed to be specifically adapted to the medical world, demonstrated impressive capacities to answer medical-exam style questions, but still needs to be evaluated in real-life. (Singhal K et al, <https://sites.research.google/med-palm/>, 2023)

To conclude, here's how playground answers when asked: **How do you foresee the role of AI in pediatric neurology?**

«Artificial intelligence (AI) has the potential to revolutionize many aspects of pediatric neurology. Here are a few ways in which AI could play a role:

1. **Diagnosis and early detection:** AI algorithms can analyze large datasets of patient records, brain imaging scans, genetic information, and other relevant data to aid in early detection and diagnosis of neurological disorders in children. This can lead to timely interventions and better outcomes.

2. **Personalized treatment plans:** AI can help develop personalized treatment plans by considering various factors such as a child's health history, genetic makeup, and response to previous therapies. By analyzing vast amounts of data, AI algorithms can suggest tailored treatment options for specific neurological conditions, enabling more effective treatment strategies.

3. **Decision support systems:** Pediatric neurologists often face complex decision-making scenarios where AI can provide valuable support. AI algorithms can help analyze medical literature, clinical guidelines, and patient data to assist doctors in making informed decisions about treatment options, medication dosages, and potential complications.

4. **Monitoring and prognosis:** AI can aid in monitoring patients with neurological disorders by processing real-time data from wearable devices, sensors, and other monitoring systems. By continuously analyzing the data, AI algorithms can detect patterns, predict disease progression, and enable early intervention.

5. **Rehabilitation.»**

All of this is true. But once again... Nothing more than non-specific, superficial and overly simplistic sen-

tences, aren't they?

While some fear that certain medical professions will rapidly disappear and be replaced by AI-driven robots, I believe that in our field of Pediatric Neurology, a personalized «human look», a long-term trustful relationship, regular and open discussions with patients will undoubtedly remain at the forefront of care in the near future. Just like patients, and like what happened with the development of Internet in its early years, we will nevertheless need to keep on learning how to use these new tools properly with our patients. Just like in any dialogue, we will need to understand that the answers given by chatboxes will largely depend on the way the question is asked... Importantly, AI tools including chatboxes will need to go through strict validation processes before they can be considered as usable in clinical practice. Some of the previously mentioned fears may be justified, time may tell. Our field of Pediatric Neurology is however so deeply characterized by repeated storytelling; active, attentive, often doubtful and subjective, but experienced human ear and eye evaluation; non-verbal language interpretation; direct observation; placement of information in a specific patient context... That increased active exchanges with our patients appear more than ever necessary to be able to make AI useful in the real world. ■

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