A 10-month-old girl was referred to our institution for evaluation of recurrent loss of consciousness that occurred for 30 seconds 1 to 3 times a day. The seizures occurred after crying, pain, or frustration. Because of tonic-like seizures before the loss of consciousness, the girl was initially remitted to pediatric neurology, where a movie-assisted electroencephalography was registered (Movie I of the online-only Data Supplement). When the girl was crying, she held breath, stiffened, and the recording showed a significant bradycardia and a 30s asystole followed by flattening of assisted electroencephalography activity and loss of consciousness consistent with anoxia. Consciousness returned rapidly after her cardiac function normalized. Between the seizures she was otherwise healthy and cardiac ultrasound and electrocardiogram (ECG) were normal. Girl was diagnosed to suffer from severe breath-holding spells.

Ambulatory ECG demonstrated similar episodes daily and a treatment with atropine (8 μg/kg, orally 3 times a day) was initiated by a pediatric cardiologist. Atropine did not significantly affect the occurrence of the spells and pharmacological treatment was changed two months later to propranolol (0.4 mg/kg 3 times a day) without any significant improvement in the incidence of the spells. Since the girl was occasionally hurt by the falls caused by loss of consciousness, an off-label treatment with levetiracetam (8 mg/kg twice a day) was started. Levetiracetam did not affect the occurrence of the breath-holding seizures, but after the treatment was initiated, breath-holding did not result in unconsciousness. Ambulatory ECG showed that her heart rate still slightly decelerated during breath-holding, but no asystole was recorded. After the girl had been spell-free for 1 month, levetiracetam was discontinued and the symptoms reappeared within few days. Levetiracetam therapy was resumed and the symptoms disappeared. However, because of the side-effects (hyperreactivity, aggressive behavior, and loss of appetite) the drug was eventually discontinued. As the symptoms were severe, implantation of permanent pacemaker was warranted.

Breath-holding spells is a relatively common disorder in young children that usually spontaneously resolves and needs no treatment. The pathogenesis is incompletely understood, but an imbalance between sympathetic and parasympathetic nervous system has been proposed. The case we present here demonstrates that levetiracetam may have significant therapeutic potential in normalizing the autonomic nervous system imbalance in this disorder. Levetiracetam is a new anticonvulsive agent that is structurally similar to the prototypical drug piracetam that has been successfully used to treat breath-holding spells. Earlier studies have suggested that piracetam stabilizes anxiety and thus diminishes spell activity. We suggest that levetiracetam may have therapeutic potential outside the central nervous system and it may modify the autonomic signaling to the heart. Levetiracetam binds to synaptic vesicle glycoprotein 2A and may also affect Ca2+/channel activity. However, the exact mechanism by which levetiracetam exerts its effects remains unknown. Since disturbed autonomic nervous system may be important in the development of cardiac arrhythmias at all ages, levetiracetam-type drugs may have novel therapeutic potential outside the treatment of epilepsy.

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Disclosures
None.

References
Recurrent Sinus Arrest and Asystole Due to Breath-Holding Spell in a Toddler; Recovery With Levetiracetam-Therapy
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