

# Alternating Hemiplegia of Childhood in Two Adult Patients with a Mild Syndrome

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**Abstract:** We describe the cognitive-behavioral functioning of two adult patients with a mild form of alternating hemiplegia of childhood (AHC). AHC is a rare, chronic neurodevelopmental syndrome manifesting in infancy or early childhood, with recurrent hemiplegic or hemidystonic attacks, various nonepileptic paroxysmal events, and cognitive-behavioral impairments, including mental delay of varying degrees. We conducted neurologic and neuroimaging examinations, as well as a neuropsychological assessment, of two men (22 and 30 years old) with mutations in the *ATPIA3* gene (p.Leu757Pro and p.Val332Glu) who were experiencing typical AHC transient episodes of alternating weakness or paralysis in order to investigate causes of their poor social functioning. During neurologic examinations of both patients, which were performed between attacks, we observed involuntary movements such as chorea and upper-limb tremor. One patient also had dysarthria. Magnetic resonance imaging revealed no parenchymal brain lesions or atrophy in either patient. Neuropsychological examinations demonstrated near-normal (patient 1) or normal (patient 2) global cognitive functioning, with some isolated executive functioning deficits. Both patients had emotional and social dysfunction as well as difficulties adapting to normal adult life. Although the clinical presentation of AHC is usually dramatic, some patients have mild forms of the syndrome (eg, no significant intellectual disability). However, motor and movement disorders, as well as coexisting emotional-affective abnormalities, may affect these patients' ability to adapt to independent life.

**Key Words:** alternating hemiplegia of childhood, cognitive functioning, mild syndrome

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AHC = alternating hemiplegia of childhood.

**A**lternating hemiplegia of childhood (AHC) is a rare, chronic neurodevelopmental syndrome estimated to

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affect approximately 1 in 1,000,000 births (Neville and Ninan, 2007). This may actually be a very conservative estimate because of the lack of sufficient knowledge about this syndrome and objective laboratory or radiologic tests confirming its diagnosis (Gergont and Kaciński, 2014; Neville and Ninan, 2007). However, genetic discoveries starting in 2012 (Heinzen et al, 2012; Rosewich et al, 2012) indicating mutation in the *ATPIA3* gene will likely lead to increased disease detection. To date, sporadic forms and a few familial cases of AHC have been detected (Masoud et al, 2017; Mikati et al, 2000; Panagiotakaki et al, 2015).

AHC is characterized by early (before 18 months of age) hemiplegic or hemidystonic attacks and various nonepileptic paroxysmal events (abnormal eye movements, paroxysmal nystagmus, dystonic attacks, episodes of autonomic disturbances). In addition, signs of permanent neurologic dysfunction such as intellectual disability, developmental delay, and/or persistent motor deficits have been observed in children with AHC (Bourgeois et al, 1993; Neville and Ninan, 2007; Rosewich et al, 2017).

Transient hemiplegic episodes are the key symptoms of AHC. The frequency of AHC attacks can range from a low of one attack every few months to a high of several times daily. Their duration can be several minutes, a couple of hours, or even a few days. Attacks can produce mild weakness or paralysis, including paralysis that can change from one moment to the next, and may feature alternating laterality during the same episode, ie, the paralysis begins unilaterally but later involves both sides or rapidly transfers to the opposite side of the body. The hemiplegia can be mixed with signs of dystonia.

Individuals typically remain conscious and alert during these attacks, although somnolence and lethargic states have also been observed. A unique aspect of these episodes is their immediate relief upon sleep, with recurrence of long-lasting bouts within 10 to 20 minutes after awakening (Kansagra et al, 2013; Masoud et al, 2017; Mikati et al, 2000; Neville and Ninan, 2007; Panagiotakaki et al, 2010, 2015). Although hemiplegic episodes may raise the possibility of Todd postictal paralysis, they are not epileptic in nature (Masoud et al, 2017; Mikati et al, 2000). However, AHC symptoms may be accompanied by true epileptic seizures (Panagiotakaki et al, 2010; Saito et al, 2010).

AHC is a very heterogeneous syndrome. Multicenter research on AHC (Panagiotakaki et al, 2010) indicates that patients vary dramatically in terms of clinical severity, episode type (plegic, tonic, autonomic, epileptic), and

accompanying symptoms. Furthermore, the natural disease course is highly variable and unpredictable within each patient. Although clinical severity appears to be constant at particular ages (except for early oculomotor abnormalities and hypotonia, which usually regress), indicating a nonprogressive nature of the disease (Neville and Ninan, 2007; Panagiotakaki et al, 2010), cases of sudden (Ito et al, 2018; Sasaki et al, 2014) or stepwise motor and/or intellectual deterioration with severe episodes have been reported (Neville and Ninan, 2007; Sasaki et al, 2014).

Many questions related to AHC have yet to be sufficiently answered. For example, little is known about the course of AHC throughout adulthood (see Ito et al, 2018), when abnormalities may become more evident or disabling. The largest knowledge gap concerns cognitive and psychosocial functioning in adults with AHC. To help fill that gap, we report the findings of our clinical evaluations of two Polish adult patients with a mild form of AHC.

### CASE REPORT

Two Polish adult patients (both men) with a relatively mild form of AHC were referred to our neurologic department for evaluation of their increasing problems with adapting to everyday life. They both provided written informed consent for their clinical data to be published.

#### Patient 1

Patient 1 was a right-handed, single, unemployed 22-year-old man. His AHC had been genetically confirmed when he was 19 (heterozygous mutation c. 2270T>C in exon 17 of *ATPIA3* gene leading to p.Leu757Pro; this was validated by bidirectional sequencing of all coding exons 1-23 of the *ATPIA3* gene, including the exon-intron boundaries, according to standard methods). The patient

had an unremarkable family history for the disease, ie, healthy parents and siblings.

#### Medical History

Both patient 1's medical records and the reports from his parents indicated that he had been born vaginally after a full-term pregnancy. His birth weight was 4.1 kg (90th percentile), birth length was 56 cm (>97th percentile), and head circumference was 35 cm (50th percentile) (percentiles from Fenton and Kim, 2013). No notable complications with the pregnancy or delivery were reported. Patient 1 started sitting at 10 months of age, which represents a slight delay according to the Denver Diagnostic Test of Psychomotor Development of the Child (Slenzak and Michalowicz, 1973). Patient 1 was able to walk unaided at 12 months and spoke his first words at 13 months. Before the age of 15 months, he required physical therapy because of muscle hypotonia.

At 15 months of age, patient 1 experienced his first sudden episode of transient right-sided hemiparesis; he did not lose consciousness. According to his parents, in the following years, he experienced similar episodes every 2 to 3 months that lasted from several minutes to 3 to 6 hours each. They also observed cases of a concomitant or independent gaze deviation at that time. At 2 years of age, patient 1 experienced involuntary abnormal choreic movements, independent of paretic attacks. As a consequence, he was hospitalized several times at the Children's Memorial Health Institute in Warsaw, Poland, and at John Paul II Upper Silesian Child Health Centre in Katowice. There he received a diagnosis based on the presentation of AHC symptoms. See Bourgeois et al (1993) for their proposed six clinical diagnostic criteria currently referred to as the Aicardi criteria. The most recent clinical AHC criteria are provided in Rosewich et al (2017). Table 1

**TABLE 1.** Comparison of Our Two Patients' Symptoms During the Three Phases of Alternating Hemiplegia of Childhood (AHC)

Phases of AHC*	Patient 1	Patient 2
Phase 1: First few months to 1 year after birth		
Mild developmental delay	+	+
Abnormal ocular movements	+	+
Episodes of dystonia or hemiplegia	+	+
Phase 2: 1 to 5 years of life		
More frequent, fluctuating hemiplegic spells	+	+
Possible loss of acquired milestones	–	–
Fixed neurologic deficits	+	+
Development of choreoathetosis	+	+
Possible occurrence of seizures	–	Treated with antiepileptic drugs
Phase 3: Age 6 years and older		
Persistent developmental delay	–	–
Fixed neurologic abnormalities	+	+
Less frequent dystonic and hemiplegic attacks	+	+
Special education, special services, residential school arrangements needed	–	+

\*The three phases are described in Mikati et al, 2000.

compares patient 1's symptoms with the most common clinical features appearing during the three phases of AHC (Mikati et al, 2000).

According to information obtained from the patient and confirmed by his family, he completed primary and secondary school without repeating any grade. He then attended a postsecondary school and studied public administration, but he never worked in this profession. At the time of hospitalization, patient 1 was unemployed and regularly attending occupational therapy sessions for adults.

In the 2 to 3 years before hospitalization, patient 1's hemiplegic attacks happened on average once a month, very rarely affected all four extremities, and lasted from 5 to 40 minutes. Triggers of the attacks included infection, emotional stress, physical fatigue, weather changes, and hunger.

Before his admission to the hospital, the patient had not been taking any long-term, ongoing medications.

### Results

Patient 1's basic body measurements on hospital admission were as follows: weight, 59 kg; height, 188 cm; body-mass index, 16.69 (falling within the underweight range); and head circumference, 56 cm. A neurologic examination revealed choreic movements in the upper limbs and mild dysarthria. There were no evident symptoms of the muscular hypotonia reported in early childhood. Basic laboratory tests showed no abnormalities. Magnetic resonance imaging of the head was normal (Figure 1A).

According to a neuropsychological assessment, patient 1's overall intellectual functioning was in the low-average range. Because of involuntary movements of the upper extremities, which prevented execution of nonverbal cognitive tasks, patient 1's functioning was evaluated using the verbal portion of the Polish version of the Wechsler Adult Intelligence Scale–Revised (Brzeziński et al, 2004). The test showed a verbal intelligence quotient of 82 (low

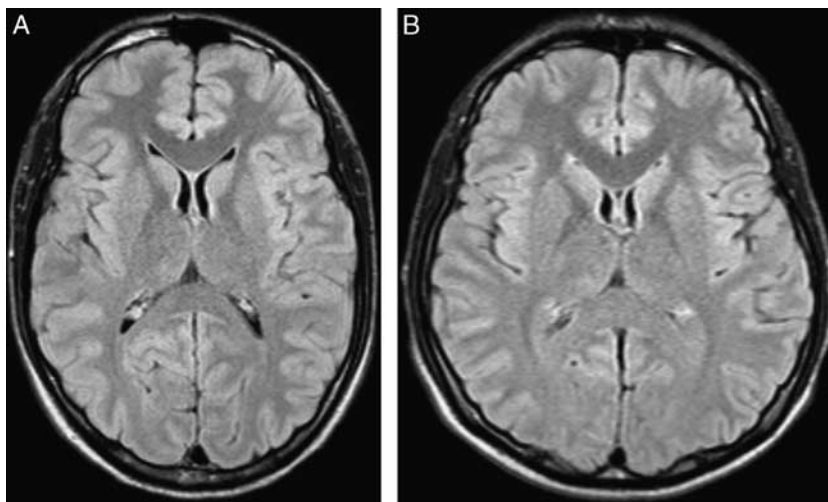
average). On the Raven's Standard Progressive Matrices (Jaworowska and Szustrowa, 2000), which measures non-verbal intellectual abilities, patient 1's test results were in the 33rd percentile (average range). Detailed analysis of his Wechsler Adult Intelligence Scale–Revised subtests suggested that he had the greatest difficulties with conceptual thinking (subtests: Vocabulary, Similarities) and both short-term and working memory (Digit Span). He also performed poorly on tasks that required problem-solving and abstract reasoning (Raven's Standard Progressive Matrices).

Assessment of patient 1's memory and learning using the Auditory Verbal Learning Test (Strauss et al, 2006) indicated average results: normal span of immediate memory, good rate of learning, and average span of delayed recall and recognition of learned material. However, a qualitative analysis showed poor organizing of information and some memory errors (perseverations and similar-sounding intrusions), which suggested difficulties with executive and controlled memory processes.

During clinical interviews and psychological testing, patient 1 manifested various behavioral abnormalities. For instance, he displayed infantile behaviors such as laughing and talking about insignificant information unrelated to the testing situation events and shortening the distance between himself and the psychologist. Impulsive reactions to irrelevant stimuli, irritability, and occasional verbally aggressive behaviors were also observed.

### Patient 2

Patient 2 was a right-handed, single, unemployed 31-year-old man who had been diagnosed in childhood with cerebral palsy (extrapyramidal choreoathetotic form) and who had AHC genetically confirmed at the age of 30 (heterozygous mutation c. 995T > A in exon 9 of *ATP1A3* gene leading to p.Val332Glu). Similarly to patient 1, patient 2 had an unremarkable family history (both parents and four sisters were healthy).



**FIGURE 1.** Cranial magnetic resonance imaging on axial fluid-attenuated inversion recovery scans from patient 1 (A) and patient 2 (B) showing no parenchymal brain lesions or atrophy.

### Medical History

According to medical records, patient 2 was born by vaginal delivery with an Apgar score of 9. He had a birth weight of 3.6 kg (50th percentile), a birth length of 56 cm (>97th percentile), and a head circumference of 34 cm (>10th percentile) (Fenton and Kim, 2013). He started sitting up at 7 months of age. At 8 months of age, however, he showed a decrease in muscle strength lasting several hours as well as breathing problems. Similar repeat episodes took place during the following month. Patient 2 spoke his first words at 14 months. He could walk independently at 18 months, which represents a delay according to the Denver Test (Slenzak and Michalowicz, 1973).

From age 2 to 12 years, patient 2 experienced right- and left-sided paresis and tetraparesis several times. These symptoms were sometimes accompanied by nystagmus homolateral to the side of the paralysis and/or difficulty with speaking and breathing. During these episodes, patient 2 did not lose consciousness and remembered everything. At age 13, he had choreoathetotic movements in the upper limbs independent of the paresis attacks. Although his electroencephalographic results never showed epileptiform abnormalities, between 14 months and 7 years of age, patient 2 was treated with antiepileptic drugs, likely based on the assumption that the paroxysmal episodes might be epileptic in nature. After that period, he did not take any long-term, ongoing medication for his symptoms.

According to patient 2's own report, he required individualized education at primary school because of his movement disorders. He graduated from high school and started studying administration at a university but did not graduate. During patient 2's childhood, he completed several psychological assessments for his educational needs. Results of his intelligence tests—the Wechsler Intelligence Scale for Children (Matczak et al, 1991) and the Polish version of the Wechsler Adult Intelligence Scale—Revised (Brzeziński et al, 2004)—were in the average range. However, psychologists noted his problems with emotional control, manifested by a tendency toward aggression, a lack of patience, and low resistance to frustration.

Patient 2 also reported that most of his paresis attacks within the past 2 to 3 years were left-sided and accompanied by speech and respiratory problems. The attacks occurred three to five times a week and lasted from a few minutes to several hours. According to his self-report, the most common provoking factors were infection, emotional stress, excitement, and physical fatigue.

### Results

Patient 2's basic body measurements on admission to the hospital were as follows: weight, 69.5 kg; height, 180 cm; body-mass index, 21.45; head circumference, 57.5 cm. A neurologic examination revealed choreoathetotic movements in the upper limbs. Basic laboratory tests showed no abnormalities. Figure 1B shows a normal magnetic resonance imaging scan of patient 2's head.

A neuropsychological assessment was consistent with patient 2's previously presented characteristics. His

intelligence level, assessed with the Raven's Standard Progressive Matrices (Jaworowska and Szustrowa, 2000), was in the average range (42nd percentile). Tests of verbal (Auditory Verbal Learning Test; Strauss et al, 2006) and nonverbal memory (Benton Visual Retention Test; Jaworowska, 2007) showed that his ability to memorize and learn new information was also normal.

Patient 2 complained that he had problems with emotional and social functioning. For example, he had tried to live independently in a big city, but this led to increased anxiety and feelings of helplessness. He therefore moved in with his sister. The family described him as a person with low self-esteem, poor social skills, and limited close interpersonal relationships. His attitude toward family members was confrontational; he often reacted with anger and was stubborn and argumentative. Results from his self-report psychological questionnaires (the Minnesota Multiphasic Personality Inventory–2; Brzezińska et al, 2012) indicated severe emotional problems such as impulsiveness, emotional lability, a tendency toward aggressive reactions, and increased anxiety and interpersonal sensitivity (Polish 72-item version of The Hopkins Symptom Checklist; Siwiak-Kobayashi, 1974). Both patient 2 and his family members reported that psychological stress and emotional excitement often led to his hemiplegic attacks.

At discharge from the hospital, patient 2 was prescribed flunarizine, a calcium channel blocker that is the most commonly used medication in AHC (eg, Brashear et al, 2018; Kansagra et al, 2013; Masoud et al, 2017; Neville and Ninan, 2007; Tenney and Schapiro, 2010). The dosage was 10 mg daily.

## DISCUSSION

Clinical descriptions of AHC rarely refer to adults because of the small number of existing long-term follow-up reports and the relatively recent identification of the genetic basis of the disorder (Ito et al, 2018; Rosewich et al, 2017).

The two case studies presented here illustrate variability in the profile of AHC in terms of type, intensity, and symptom fluctuation during the life course of the patients, as well as some atypical clinical signs. Both patients, before the age of 18 months, experienced transient episodes of alternating weakness or paralysis that affected either one or both sides of the body, or else transferred from one side to the other (Bourgeois et al, 1993). In accordance with the disease course (Masoud et al, 2017; Mikati et al, 2000; Neville and Ninan, 2007; Panagiotakaki et al, 2010, 2015), the patients' hemiplegic attacks persisted for varying periods of time, decreased with age, abated with sleep, and were not associated with consciousness disorders. Patients with AHC may also have greater involvement of one side of the body and coexisting autonomic phenomena (Panagiotakaki et al, 2010). This was seen in patient 2.

According to clinical criteria (Bourgeois et al, 1993; Rosewich et al, 2017), the patients' neurologic examinations, which took place between plegic attacks, indicated abnormalities. Both patients developed involuntary movements,

including chorea and tremor of the upper limbs. Additionally, the first patient had dysarthria. Various extrapyramidal signs, as well as ataxia, dystonia, or dysarthria (Kansagra et al, 2013; Mikati et al, 2000; Panagiotakaki et al, 2010), are frequent in AHC and often contribute to a misdiagnosis of cerebral palsy, especially during early life stages (Mikati et al, 2000). Fine motor skill abnormalities usually increase or become more evident with age and, therefore, are present in the majority of adult patients (Bourgeois et al, 1993; Panagiotakaki et al, 2010).

Despite unique clinical pictures, both patients presented with a relatively mild syndrome. Whereas people with AHC usually have evident delays in psychomotor and language development and rarely walk independently before the age of 2 (Panagiotakaki et al, 2010, 2015), our patients had only a mild delay in achieving basic motor milestones during the first year of life. The patients started walking independently by 12 and 18 months, respectively, and their gross motor abilities remained functionally constant over time. Research suggests that the majority of patients with AHC have an ataxic gait, and gross motor abnormalities persist until adulthood (Panagiotakaki et al, 2010, 2015).

These two patients' global intellectual functioning is remarkable in the context of AHC. Results from our intellectual assessments for patient 1 suggested an average or low-average range of intellect (depending on the task), and results for patient 2 suggested an average range of intellect. Both patients completed secondary school without repeating any grades. Normal or near-normal mental development in patients with AHC is rare. Mikati and colleagues (2000) described only 4 children in a group of 44 with cognitive functioning in the normal range. One of the largest AHC studies reported that at least 92% of affected patients exhibited some degree of intellectual dysfunction, either mild (18%), moderate (50%), or severe (24%) (Panagiotakaki et al, 2010). In a longitudinal study, Mikati et al (2000) found a relationship between early onset of AHC and more severe intellectual deficits; Silver and Andermann (1993) observed that intellectual functioning is correlated with age, with clear declines noticeable during the first 10 years.

In contrast to our findings of a normal or near-normal intelligence quotient, detailed neuropsychological examinations revealed minor deficits in executive functioning, including poor planning, inaccurate problem-solving, and poor performance on fluency tasks that required executive control. Both patients also displayed poor adaptation and adjustment to new situations, along with limited social-cognitive functioning. Although little has been published about executive deficits among patients with AHC, one study did find impairments of neuropsychological functioning in children with AHC (Shafer et al, 2005). To our knowledge, there is no similar description in adults with AHC. This is an important research gap because early adulthood is the period of life when executive functions typically reach full development (Best and Miller, 2010). Abnormalities during this stage of life become more apparent because of the need for better planning of, and control over, one's behavior in order to live independently and meet larger psychosocial demands.

The level of emotional functioning displayed by our patients provides insight into how AHC can affect adults. Behavioral outbursts, impulsivity, and emotional-affective abnormalities are frequent in patients with AHC (Brashear et al, 2018) and are usually similar to problems observed in patients with attention-deficit hyperactivity disorder (Masoud et al, 2017). Impulsiveness, argumentative behaviors, irritability, and aggression usually lead to conflicts and social isolation. We observed these features in both of our patients. However, some emotional issues (especially with regard to patient 2) might be secondary to observed physical dysfunction. Certain emotional problems could thus be partially explained as adaptation problems that are present in cognitively normal individuals who experience serious motor disabilities. Paroxysmal and nonparoxysmal motor disorders significantly disrupt one's daily life, affect one's ability to learn, and influence participation in various activities. As a consequence of such disruptions, our patients were unemployed, even though their intellectual abilities suggest that they have the capacity to work. Attempts taken by patient 2 to live independently failed as a result of growing emotional and social problems. Physical or psychological stress, along with excitement, often emerge as hemiplegic episode triggers (Neville and Ninan, 2007; Rosewich et al, 2014). Long-lasting and alternating hemiplegic attacks, preceded especially by stressful situations, may sometimes suggest psychogenic disorders as additional reactions. Therefore, more information regarding mental correlates (both primary and secondary) of this syndrome is required to facilitate more targeted treatment (Shafer et al, 2005).

Findings related to clinical and genetic features of patients with AHC are very interesting. Research shows that more than 80% of patients with AHC have pathogenic variants in the *ATP1A3* gene, and mutations are more commonly de novo than inherited (Brashear et al, 2018). *ATP1A3* codes for the  $\alpha$  3 subunit of the p-type  $\text{Na}^+/\text{K}^+$ -ATPase protein, which is highly expressed in the cortex, hippocampus, basal ganglia, thalamus, and cerebellum (Masoud et al, 2017). In a study involving a large series of patients with AHC, Panagiotakaki and colleagues (2015) identified 34 different mutations in the *ATP1A3* gene that are responsible for normal neural cell functioning. Genotype-phenotype correlations of the three major mutations suggest that the p.Glu815Lys mutation (16%) is associated with earlier AHC onset, and the most severe phenotype—p.Asp801Asn (43%)—appears to confer a milder phenotypic expression. Finally, p.Gly947Arg (11%) appears to correlate with the most favorable prognosis (Panagiotakaki et al, 2015).

In terms of intellectual functioning, a majority of p.Glu815Lys patients have severe or moderate disability, p.Asp801Asn patients most often present with moderate disability, and p.Gly947Arg patients usually develop only mild disabilities (Panagiotakaki et al, 2015). The mutation observed in patient 1 (c. 2270T>C; p.Leu757Pro) has been previously described by Rosewich and colleagues (2014) as an *ATP1A3*-36 condition associated with some intellectual disabilities, choreoathetosis, and dysarthria. The mutation identified in patient 2 (c. 995T>A;

p.Val332Glu) has not been described previously. However, numerous in silico analyses (PolyPhen-2, MutationTaster, Provean, Meta-SNP) indicate that the reported *ATPIA3* gene mutation is very likely pathogenic.

In summary, because AHC is a unique, rare, and highly variable syndrome, its diagnosis is difficult and usually delayed. Most clinical descriptions of the syndrome refer to children. The natural history of AHC is difficult to predict, and some symptoms may develop or become more apparent with age, especially within the cognitive-behavioral domain. Therefore, more clinical observations of AHC evolution in adulthood are needed.

Although the clinical presentation of AHC is usually dramatic, some patients have mild forms of the syndrome (eg, without evident intellectual disabilities), and some do not fulfill all established criteria or present with unusual signs. In this context, relationships between phenotypic variations of AHC and *ATPIA3* mutations are quite interesting. Early detection of mild and atypical AHC cases is important in order to limit unnecessary workups, initiate treatment, and provide appropriate therapeutic interventions. Treatments should be tailored to individual needs in terms of special education, physical and psychosocial therapies, and/or psychotherapeutic services. Psychological support can be especially important in adults with relatively good intellectual functioning. Motor and movement disorders, and coexisting emotional-affective abnormalities, may significantly affect their ability to live independently.

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#### REFERENCES

- Best JR, Miller PH. 2010. A developmental perspective on executive function. *Child Dev.* 81:1641–1660.
- Bourgeois M, Aicardi J, Goutieres F. 1993. Alternating hemiplegia of childhood. *J Pediatr.* 122:673–679.
- Brashear A, Sweadner KJ, Cook JF, et al. 2018. *ATPIA3*-related neurologic disorders. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, eds. *GeneReviews® [Internet]*. Seattle, Washington: University of Washington, Seattle; 1993–2018. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1115/>.
- Brzezińska U, Koć-Januchta M, Stańczak J. 2012. *Minnesocki Wielowymiarowy Inwentarz Osobowości-2–MMPI®-2 [Minnesota Multiphasic Personality Inventory-2]*. Warsaw, Poland: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- Brzeziński J, Gaul M, Hornowska E, et al. 2004. *Skala Inteligencji Wechslera dla Dorosłych–Wersja Zrewidowana [Wechsler Adult Intelligence Scale]*. Warsaw, Poland: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- Fenton TR, Kim JH. 2013. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatr.* 13:59.
- Gergont A, Kaciński M. 2014. Alternating hemiplegia of childhood: new diagnostic options. *Neurol Neurochir Pol.* 48:130–135.
- Heinzen EL, Swoboda KJ, Hitomi Y, et al. 2012. De novo mutations in *ATPIA3* cause alternating hemiplegia of childhood. *Nat Genet.* 44:1030–1034.
- Ito T, Narugami M, Egawa K, et al. 2018. Long-term follow up of an adult with alternating hemiplegia of childhood and a p.Gly755Ser mutation in the *ATPIA3* gene. *Brain Dev.* 40:226–228.
- Jaworowska A. 2007. *Test Pamięci Wzrokowej Bentona–Wydanie piąte [The Benton Visual Retention Test]*. Warsaw, Poland: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- Jaworowska A, Szustrowa T. 2000. *TMS-K–Test Matryce Ravena w Wersji Standard–forma Klasyczna [Raven’s Standard Progressive Matrices]*. Warsaw, Poland: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- Kansagra S, Mikati MA, Vigevano F. 2013. Alternating hemiplegia of childhood. *Handb Clin Neurol.* 112:821–826.
- Masoud M, Prange L, Wuchich J, et al. 2017. Diagnosis and treatment of alternating hemiplegia of childhood. *Curr Treat Options Neurol.* 19:8.
- Matczak A, Piotrowska A, Ciarkowska W. 1991. *WISC: Skala Inteligencji Wechslera dla Dzieci [WISC: The Wechsler Intelligence Scale for Children]*. Warsaw, Poland: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
- Mikati MA, Kramer U, Zupanc ML, et al. 2000. Alternating hemiplegia of childhood: clinical manifestations and long-term outcome. *Pediatr Neurol.* 23:134–141.
- Neville BG, Ninan M. 2007. The treatment and management of alternating hemiplegia of childhood. *Dev Med Child Neurol.* 49:777–780.
- Panagiotakaki E, De Grandis E, Stagnaro M, et al. 2015. Clinical profile of patients with *ATPIA3* mutations in alternating hemiplegia of childhood—a study of 155 patients. *Orphanet J Rare Dis.* 10:123.
- Panagiotakaki E, Gobbi G, Neville B, et al. 2010. Evidence of a non-progressive course of alternating hemiplegia of childhood: study of a large cohort of children and adults. *Brain.* 133:3598–3610.
- Rosewich H, Ohlenbusch A, Huppke P, et al. 2014. The expanding clinical and genetic spectrum of *ATPIA3*-related disorders. *Neurology.* 82:945–955.
- Rosewich H, Sweney MT, DeBrosse S, et al. 2017. Research conference summary from the 2014 International Task Force on *ATPIA3*-Related Disorders. *Neurol Genet.* 3:e139.
- Rosewich H, Thiele H, Ohlenbusch A, et al. 2012. Heterozygous de-novo mutations in *ATPIA3* in patients with alternating hemiplegia of childhood: a whole-exome sequencing gene-identification study. *Lancet Neurol.* 11:764–773.
- Saito Y, Inui T, Sakakibara T, et al. 2010. Evolution of hemiplegic attacks and epileptic seizures in alternating hemiplegia of childhood. *Epilepsy Res.* 90:248–258.
- Sasaki M, Ishii A, Saito Y, et al. 2014. Genotype-phenotype correlations in alternating hemiplegia of childhood. *Neurology.* 82:482–490.
- Shafer ME, Mayfield JW, McDonald F. 2005. Alternating hemiplegia of childhood: a study of neuropsychological functioning. *Appl Neuropsychol.* 12:49–56.
- Silver K, Andermann F. 1993. Alternating hemiplegia of childhood: a study of 10 patients and results of flunarizine treatment. *Neurology.* 43:36–41.
- Siwiak-Kobayashi M. 1974. *Kliniczna Lista Objawów [72-Item version of The Hopkins Symptom Checklist]*. Warsaw, Poland: Instytut Psychiatrii i Neurologii.
- Slenzak J, Michalowicz R. 1973. Denver test—diagnostic test of psychomotor development of the child. *Probl Med Wieku Rozwoj.* 3:47–76.
- Strauss E, Sherman EMS, Spreen O. 2006. Rey Auditory Verbal Learning Test (RAVLT). In: Strauss E, Sherman EMS, Spreen O, eds. *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*, 3rd ed. Oxford, United Kingdom: Oxford University Press; 776–810.
- Tenney JR, Schapiro MB. 2010. Child neurology: alternating hemiplegia of childhood. *Neurology.* 74:e57–e59.