Alice in Wonderland syndrome
A systematic review
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Abstract
Purpose of review: To summarize the literature on Alice in Wonderland syndrome (AIWS), a disorder characterized by distortions of visual perception, the body schema, and the experience of time. Recent findings: On the basis of 169 published case descriptions, the etiology of AIWS is divided into 8 main groups, with neurologic disorders affecting mostly adults and elderly patients and encephalitides affecting mostly patients aged \( \leq 18 \) years. Symptoms of AIWS are also experienced in the general population, with up to 30% of adolescents reporting nonclinical symptoms. Summary: In clinical cases of AIWS, auxiliary investigations (including blood tests, EEG, and brain MRI) are strongly advised. Treatment should be directed at the suspected underlying condition, although reassurance that the symptoms themselves are not harmful seems to suffice in about 50% of the cases. International classifications such as the DSM and ICD should consider placing the syndrome on their research agenda.

F
irst described in 1955, Alice in Wonderland syndrome (AIWS) is a perceptual disorder characterized by distortions of visual perception (metamorphopsias), the body schema, and the experience of time. The name refers to Lewis Carroll’s well-known children’s book Alice’s Adventures in Wonderland, in which Alice feels (among other things) her body growing both larger and smaller (figures 1 and 2). After 60 years of relative obscurity, AIWS has begun to receive scientific attention. This renewed interest is in part because of the current possibility to explore the brain’s networks responsible for mediating its symptoms with the aid of functional imaging techniques. AIWS symptoms have both diagnostic and therapeutic consequences that differ substantially from those in schizophrenia spectrum disorders and other
hallucinatory syndromes. This article presents an overview of the literature on AIWS published over the past 60 years and summarizes its implications for clinical practice and research.

METHODS
A systematic literature search was carried out in PubMed (until June 2015) using the search terms “Alice in Wonderland syndrome,” “syndrome of Alice in Wonderland,” and variants thereof. Included were articles in the English, Dutch, German, French, Spanish, and Italian languages. All cross-references were checked systematically. In this

Figure 1  Alice experiences total-body macrosomatognosia. Illustration by John Tenniel (1865)

Figure 2  (A) Alice experiences partial macrosomatognosia, and (B) Alice experiences total-body microsomatognosia. Illustrations by John Tenniel (1890).
| Condition                                               | No. of case reports (%) in total group (N = 166) | No. of case reports (%) in patients aged ≤18 y | No. of case reports (%) in patients aged >18 y |
|---------------------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Infectious diseases                                     | 38 (22.9)                                    | 36 (21.7)                                     | 2 (1.2)                                       |
| Coxsackie B1 virus encephalitis                         | 2 (1.2)                                      | 2 (1.2)                                       | —                                             |
| Cytomegalovirus                                         | 1 (0.6)                                      | 1 (0.6)                                       | —                                             |
| Epstein-Barr virus encephalitis (mononucleosis infectious) | 26 (15.7)                                    | 24 (14.5)                                     | 2 (1.2)                                       |
| Influenza A virus encephalitis                          | 3 (1.8)                                      | 3 (1.8)                                       | —                                             |
| Lyme neuroborreliosis                                   | 1 (0.6)                                      | 1 (0.6)                                       | —                                             |
| Scarlet fever                                           | 1 (0.6)                                      | 1 (0.6)                                       | —                                             |
| Typhoid encephalopathy                                 | 1 (0.6)                                      | 1 (0.6)                                       | —                                             |
| Varicella-zoster encephalitis                           | 3 (1.8)                                      | 3 (1.8)                                       | —                                             |
| CNS lesions                                              | 13 (7.8)                                     | 3 (1.8)                                       | 10 (6.0)                                      |
| Acute disseminated encephalomyelitis                    | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Cavernous angioma                                       | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Cerebral arteriosclerosis                               | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Cerebral thrombosis                                     | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Cerebral hemorrhage                                     | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Cerebral infarction                                     | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Brain tumor                                             | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Microembolization after open heart surgery               | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Robin Hood syndrome                                     | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Traumatic encephalopathy                               | 3 (1.8)                                      | 3 (1.8)                                       | —                                             |
| Wallenberg syndrome                                     | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| PNS lesions                                              | 2 (1.2)                                      | —                                             | 2 (1.2)                                       |
| Eye disease                                             | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Middle-ear disease                                      | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Paroxysmal neurologic disorders                         | 51 (30.7)                                    | 33 (19.9)                                     | 18 (10.8)                                     |
| Epilepsy                                                | 5 (3.0)                                      | 4 (2.4)                                       | 1 (0.6)                                       |
| Headache with neurologic deficits and CSF lymphocytosis | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Migraine                                                | 45 (27.1)                                    | 29 (17.5)                                     | 16 (9.6)                                      |
| Psychiatric disorders                                   | 6 (3.6)                                      | —                                             | 6 (3.6)                                       |
| Depressive disorder                                     | 2 (1.2)                                      | —                                             | 2 (1.2)                                       |
| Derealization/depersonalization disorder                 | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Misidentification syndrome                              | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Schizophrenia                                           | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Schizoaffective disorder                                | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Medication                                              | 10 (6.0)                                     | 4 (2.4)                                       | 6 (3.6)                                       |
| 5-HT₂ antagonist                                        | 1 (0.6)                                      | —                                             | 1 (0.6)                                       |
| Dextromethorphan                                        | 1 (0.6)                                      | 1 (0.6)                                       | —                                             |

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article, symptoms of AIWS experienced by patients diagnosed with a neurologic, psychiatric, or other medical condition are referred to as "clinical," and symptoms of AIWS experienced by individuals in the general population who have not sought medical attention are referred to as “nonclinical.”

**RESULTS**

The search terms yielded 130 hits in PubMed. Of these, 59 articles had AIWS as their main subject. Via cross-references an additional 11 articles were found, yielding a total of 70 articles. Of these, more than 50% were published during the prior decade. A total of 170 patients were described, 20 from one case series and 48 from another case series. The majority of the remaining articles consisted of individual case descriptions. Because one patient was described twice, the total number of original case descriptions was 169. Patient sex was mentioned for 162 patients; 55.6% of them were male. Age was mentioned in 166 patients; mean age was 15.5 years. A total of 132 patients were ≤18 years, with a mean age of 9 years, and 34 patients were 19 years and older, with a mean age of 40 years. Table 1 presents an overview of the many disorders, intoxications, and other conditions that have been described in the context of AIWS. Among youths, the most frequently described condition was encephalitis (21.7% vs 1.2% among adults.

| Condition                                | No. of case reports (%) in total group (N = 166) | No. of case reports (%) in patients aged ≤18 y | No. of case reports (%) in patients aged >18 y |
|------------------------------------------|--------------------------------------------------|-------------------------------------------------|------------------------------------------------|
| Cough syrup (containing dihydrocodeine and DL-methylephedrine) | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Montelukast                               | 1 (0.6)                                          | 1 (0.6)                                         | —                                               |
| Oseltamivir                               | 1 (0.6)                                          | 1 (0.6)                                         | —                                               |
| Risperidone                               | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Topiramate                                | 4 (2.4)                                          | 1 (0.6)                                         | 3 (1.8)                                         |
| Substance-induced (HPPD)                 | 10 (6.0)                                         | 1 (0.6)                                         | 9 (5.4)                                         |
| Amanita muscaria                          | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Amphetamines                              | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Ayahuasca                                 | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Cannabis                                  | 1 (0.6)                                          | 1 (0.6)                                         | —                                               |
| Cocaine                                   | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| LSD                                       | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| MDMA                                      | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Mescaline                                 | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Toluene-containing solvent                | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Trichlorethylene                          | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Miscellaneous                             | 5 (3.0)                                          | —                                               | 5 (3.0)                                         |
| Hypnagogic state                          | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Hypnopompic state                         | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Hypnotherapy                              | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Hyperpyrexia                              | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |
| Sensory deprivation                       | 1 (0.6)                                          | —                                               | 1 (0.6)                                         |

Abbreviations: HPPD = hallucinogen persisting perception disorder; PNS = peripheral nervous system.
and elderly patients), with the Epstein-Barr virus being the most frequently reported pathogen (68.4% of all cases of encephalitis). Among the group of adults and elderly patients, neurologic disorders were most frequently described (16.8%); of all these disorders, migraine was the most prevalent condition (9.6%). The course and outcome were described in 150 patients. In 54 patients (36.0%) the treatment regimen was also specified; this mostly involved pharmacologic treatment aimed at alleviating the underlying condition. One patient received electroconvulsive treatment\(^1\) and another patient received repetitive transcranial magnetic stimulation\(^2\); both treatments were successful. The remaining patients received no treatment or it was unspecified. Full remission was obtained in 46.7% of all patients, and partial or temporary remission in 11.3%. In chronic conditions such as epilepsy and migraine, full remission was obtained only rarely.

**DISCUSSION**

**Historical perspective**

The term Alice in Wonderland syndrome was introduced in 1955 by the British psychiatrist John Todd (1914–1987) to cover a group of symptoms “… intimately associated with migraine and epilepsy, although not confined to these disorders.”\(^12\) As envisioned by Todd,\(^12\) the group comprised derealization, depersonalization, hyperschematia, hyposchematia, and somatopsychic duality, as well as illusory changes in the size, distance, or position of stationary objects in the visual field; illusory feelings of levitation; and illusory alterations in the sense of the passage of time. Incidentally, Todd was well aware that he was not the first to describe those individual symptoms. Many of them had appeared before in the literature on hysteria,\(^13\)–\(^17\) on general neurology,\(^14\)–\(^17\) and on soldiers with occipital wounds after World Wars I and II.\(^18\),\(^19\) Moreover, in 1933 and 1952, Coleman\(^20\) and Lippman,\(^21\) respectively, had already drawn comparisons between those symptoms and the experiences of Alice in Wonderland, albeit without turning the name into an eponym. Lippman\(^21\) was also the first to suggest that the bodily changes experienced by Alice might well be inspired by body schema illusions Lewis Carroll had experienced himself. Carroll (pseudonym of the British mathematician Charles Lutwidge Dodgson, 1832–1898) had migraines, and his diaries indicate that his attacks were sometimes preceded by aural phenomena.\(^22\) However, historians consider Lippman’s hypothesis inconclusive, as the diaries fail to demonstrate that Dodgson experienced any aural phenomena before he wrote his book.\(^23\) An alternative hypothesis is that Dodgson had knowledge of—or perhaps had experimented with—the hallucinogenic mushroom *Amanita muscaria*.\(^24\) Whatever the exact course of events may have been, with Alice in Wonderland, Dodgson created a character that appealed as much to physicians as it did to the book’s intended audience. And Todd, by adopting the name, chose a memorable moniker for a group of symptoms hitherto described in isolation of each other.

**Phenomenology**

Over the past 60 years, AIWS symptoms have come to include 42 visual symptoms (table 2) and 16 somesthetic and other nonvisual symptoms (table 3). What these symptoms have in common with each other is that they constitute distortions of sensory perception rather than hallucinations or illusions.\(^25\) Hallucinations are percepts experienced in the absence of an appropriate stimulus from the outside world, such as a voice heard in the absence of sound.
| Type of metamorphopsia                  | Characterization                                                                 | No. of times (%) described in the literature (N = 169) |
|----------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------|
| Achromatopsia                          | The inability or strongly diminished ability to perceive color                      | 9 (5.3)                                                |
| Akinetopsia                           | The inability to perceive motion                                                   | —                                                      |
| Arugopsia                              | Seeing wrinkled surfaces as smooth                                                 | 1 (0.6)                                                |
| Chloropsia                             | Green vision                                                                      | —                                                      |
| Chromatopsia                           | Seeing things in a single hue (as in chloropsia, cyanopsia, erythropsia, ianothinopsia, and xanthopsia) | 1 (0.6)                                                |
| Corona phenomenon                      | An extra contour around objects                                                    | —                                                      |
| Cyanopsia                              | Blue vision                                                                       | —                                                      |
| Dyschromatopsia                        | Color confusion                                                                    | 3 (1.8)                                                |
| Dysmegalopsia                          | A diminished ability to appreciate the size of objects                             | —                                                      |
| Dysmetropsia                           | A change in the apparent size and distance of objects                             | —                                                      |
| Dysmorphism                            | Lines and contours appearing to be wavy                                           | 34 (20.1)                                              |
| Dysplaptopsia                          | Objects appearing flattened and elongated                                          | —                                                      |
| Enhanced stereoscopic vision           | An exaggeration of the depth and detail of visually perceived objects             | 2 (1.2)                                                |
| Entomopia                              | Seeing multiple images, as if perceived through an insect’s eye                     | —                                                      |
| Erythropsia                            | Red vision                                                                        | 3 (1.8)                                                |
| Gyropsia                               | Seeing an illusory, circular movement                                             | —                                                      |
| Hemimetamorphopsia                     | A visual distortion of only one half of an object                                  | —                                                      |
| Hyperchromatopsia                      | Seeing colors as exceptionally bright                                             | 4 (2.4)                                                |
| Ianothinopsia                          | Purple vision                                                                     | 1 (0.6)                                                |
| Illusory splitting                     | An illusory vertical splitting of objects                                          | 1 (0.6)                                                |
| Illusory visual spread                 | A perceived extension, expansion, or prolongation of objects                       | —                                                      |
| Inverted vision                        | Objects appearing rotated (usually in the coronal plane, over 90° or 180°)        | 1 (0.6)                                                |
| Kinetopsia                             | Illusory movement                                                                  | 15 (8.9)                                               |
| Loss of stereoscopic vision            | Objects appearing 2-dimensional or “flat”                                          | —                                                      |
| Macroproxiopia                         | Objects appearing larger and closer by than they are                               | 2 (1.2)                                                |
| Macropsia                              | Seeing things larger than they are                                                | 76 (45.0)                                              |
| Micropsia                              | Seeing things smaller than they are                                               | 99 (58.6)                                              |
| Microtelepsia                          | Objects appearing smaller and farther away than they are                            | 7 (4.1)                                                |
| Monocular metamorphopsia               | Metamorphopsia for one eye                                                         | —                                                      |
| Mosaic vision                          | A fragmentation of perceived objects into irregular, crystalline, polygonal facets, interlaced as in a mosaic | —                                                      |
| Palinopsia                             | Illusory recurrence of visual percepts (as in polyopia, illusory visual spread, and the trailing phenomenon) | 3 (1.8)                                                |
| Pelopsia                               | Objects appearing closer by than they are                                         | 11 (6.5)                                               |
| Plagiopsia                             | Objects appearing as if tilted                                                     | —                                                      |
| Polyopia                               | Seeing multiple identical copies of a single image                                 | 1 (0.6)                                                |
| Porropsia                              | Stationary objects appearing to move away                                          | 3 (1.8)                                                |
| Prosopometamorphopsia                  | Apparent distortion of faces                                                      | 3 (1.8)                                                |

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production or a cat seen that is not there. Illusions do have a source in the outside world, albeit one that is (often fleetingly) misperceived or misinterpreted. Thus music may be heard in the drone of passing traffic and a curtain moving in the wind may be mistaken for an intruder. Like illusions, distortions are based on sensory impressions, but they feature highly specific changes in highly specific aspects of the sensory input picture. For example, all straight lines may be perceived as wavy (dysmorphopsia), all vertical lines as slanted (plagiopsia), all stationary objects as moving (kinetopsia), or all eyes as unnaturally big (prosopometamorphopsia). Tables 2 and 3 describe the many possible variants and also how often they have been described in case reports of AIWS. Strikingly, micropsia and macropsia have been described most frequently in the literature (in 58.6% and 45.0% of all patients, respectively), which might indicate that they are the most prevalent types of distortion but also that they are the best known and therefore studied most frequently.

The duration of symptoms of AIWS tends to be short, mostly on the order of minutes to days\(^2^6\); however, symptoms may also persist for years\(^2\) or even be lifelong.\(^2^7\) A salient detail is that after visual fixation on an object, metamorphopsias may sometimes arise after an interval of seconds to minutes.\(^2^7,2^8\) After that temporal delay, objects are perceived in a distorted manner, but during the delay the perceptual process is undisturbed. In the historical literature this phenomenon has been explained as a sign of cerebral asthenopia\(^2^8,2^9\) (i.e., an unusual fatigability of the perceptual system).

### Epidemiology

No epidemiologic data on AIWS in the population at large are available. Although it is generally assumed that the syndrome is rare, clinical studies among patients with migraine indicate that the prevalence rate in this group may be around 15%.\(^2^3,3^0\) Moreover, some studies indicate that individual symptoms of AIWS are not rare in the general population. A cross-sectional study of 1,480 adolescents\(^3^1\) found a lifetime prevalence of micropsia and/or macropsia of 5.6% for males and 6.2% for females. A second cross-sectional study of 3,224 high school students\(^3^2\) found 6-month prevalence rates of 3.8% for micropsia, 3.9% for macropsia, 2.5% for protracted duration, and 1.3% for the quick-motion phenomenon. A third cross-sectional study\(^3^3\) of 297 individuals with a median age of 25.7 years found lifetime prevalence rates of 30.3% for teleopsia, 18.5% for dysmorphopsia, 15.1% for macropsia, and 14.1% for micropsia. This study also showed that 38.9% of the affected individuals experienced a single symptom, 33.6% experienced 2, 10.6% experienced 3, and 16.8% experienced 4. This buildup might indicate a common underlying etiologic process responsible for the mediation of all 4 symptoms or a stochastic process in which the presence of one symptom lowers the threshold for another one to join in.
Pathophysiology

The symptoms of AIWS are attributed to functional and structural aberrations of the perceptual system. On the whole, central pathology is considered the most prevalent cause; however, dysmorphopsia, for example, is also experienced in the context of retinal ablation and some other types of eye disease, and plagiopsia (visual tilt) is also experienced in the context of labyrinthine disease. Nevertheless, most symptoms of AIWS are attributed to centrally located neuron populations and even cell columns that respond selectively to specific types of sensory input (for vision, notably cortical areas V1–V5).

Area V4 of the extrastriate visual cortex, for example, responds selectively to color, whereas area V5 responds to movement. Both areas also respond to shape and depth, but bilateral loss of function of V4 results in achromatopsia (the inability to see color) and bilateral loss of V5 results in akinetopsia (the inability to see motion). The inability to visually perceive vertical lines (plagiopsia) or lines under a different angle is attributed to loss of function of orientation columns that are grouped together throughout the horizontal layers of visual cortex. Similarly, various neuron populations have been identified as being responsible for mediating different types of metamorphopsia, and for other metamorphopsias educated guesses have been made. Sometimes this involves higher-order mismatches between larger components of the visual network, which can vary interindividually. An example of the latter situation can be found in complex types of prosopometamorphopsia, in which human faces may be perceived consistently as animal faces, and even in an apparently straightforward symptom such as micropsia, which was found to be associated with a consistent pattern of occipital hypoactivation and parietal hyperactivation in an fMRI study.

Table 3  Somesthetic and other nonvisual distortions that may be experienced in the context of Alice in Wonderland syndrome

| Type of distortion | Characterization                                              | No. of times (%) described in the literature (N = 169) |
|--------------------|---------------------------------------------------------------|--------------------------------------------------------|
| Aschematia         | Inadequate representation of the space occupied by some part of the body | 1 (0.6)                                                |
| Derealization      | Experiencing the world as unreal                              | 17 (10.0)                                              |
| Depersonalization  | Experiencing oneself as unreal                                 | 7 (4.1)                                                |
| Hyperschematia     | Overrepresentation of the space occupied by some part of the body | 1 (0.6)                                                |
| Hyposchematia      | Underrepresentation of the space occupied by some part of the body | —                                                      |
| Illusory feeling of levitation | Sensation of floating in the air                               | 4 (2.4)                                                |
| Palisomesthesia    | Illusory recurrence of somesthetic percepts                   | —                                                      |
| Paraschematia      | Inappropriate representation of the space occupied by some part of the body | —                                                      |
| Partial macrosomatognosia | Experiencing a part of the body as larger than it is       | 12 (7.1)                                               |
| Partial microsomatognosia | Experiencing a part of the body as smaller than it is     | 13 (7.7)                                               |
| Protracted duration | Deceleration of psychological time                           | 6 (3.6)                                                |
| Quick-motion phenomenon | Acceleration of psychological time                         | 22 (13.0)                                              |
| Splitting of the body image | Sensation of one’s own body being split in 2, usually down the middle | 1 (0.6)                                                |
| Time distortion    | Altered experience of psychological time                     | 3 (1.8)                                                |
| Total-body macrosomatognosia | Experiencing the whole body as larger than it is       | 15 (8.9)                                               |
| Total-body microsomatognosia | Experiencing the whole body as smaller than it is    | 14 (8.3)                                               |
Whenever treatment is considered useful and necessary, it needs to be aimed at the suspected underlying condition.

Mutatis mutandis, the same would seem to hold true for somesthetic distortions, in the sense that functional and/or structural aberrations of specific neuron populations in somatosensory cortical areas are responsible for mediating body schema illusions such as microsomatognosia, palisomesthesia, aschematia, etc. In these cases, parts of the network located around the parieto-temporo-occipital junction are responsible, although here too a mismatch between higher-order components of the network as a whole may be at play, as in ischemia of distal parts of the anterior cerebral arteries that supply parts of the perceptual network responsible for integrating composite sensory data for awareness of the body schema. Whether similar mechanisms are responsible for mediating time distortions is as yet unknown.

Etiology
The conditions responsible for mediating the symptoms of AIWS are legion. Table 1 presents those described so far in the literature, classified into 8 main groups. One of those groups is “substance-induced,” also known as hallucinogen persisting perception disorder (HPPD), a nosologic construct featured in the DSM-5 and other classifications as a separate diagnostic category that covers perceptual symptoms that arise during (or after the cessation of) the use of illicit substances. The list of conditions associated with AIWS is long and is expected to grow even longer when more cases and case series are published.

Diagnosis and differential diagnosis
AIWS does not feature in major classifications such as the ICD-10 and the DSM-5. As a consequence, in clinical practice the diagnosis of AIWS stands and falls with proper history-taking, a thorough physical (including neurologic and often otologic and/or ophthalmic) examination, and sound knowledge of the many and varying symptoms characteristic of AIWS and their possible causes. Cases with a suspected central origin should prompt auxiliary investigations including blood tests, EEG, and brain MRI scan, even though the chances of finding any demonstrable lesions are generally considered to be low.

The differential diagnosis of AIWS and its individual symptoms is complex, as it involves at least 3 levels of conceptualization. First, the symptoms need to be distinguished from other positive disorders of perception such as hallucinations and illusions, with which they may be easily confused. Second, their most likely cause needs to be established. As table 1 indicates, many diagnoses are possible. Therefore, third, whether the diagnosed condition may be responsible for mediating the symptoms must be established. Because metamorphopsias and other distortions are also experienced by individuals in the general population, situations may arise in which the disorder diagnosed is not causally connected with the symptoms at hand or in which a therapeutic intervention turns out to be the actual cause.

Treatment and prognosis
Most nonclinical and clinical cases of AIWS are considered benign, in the sense that full remission of the symptoms can often be obtained, sometimes spontaneously and in other cases after proper treatment. However, in clinical cases with an underlying chronic condition (such as migraine and epilepsy), symptoms tend to recur in concordance with active phases of the disease, and in cases of encephalitis the prognosis may also vary. As a consequence, the need to treat requires careful assessment, proper knowledge of the natural course of the various underlying conditions that are possible, and a careful explanation to the patient of what to expect from which therapeutics under which circumstances. In many cases reassurance will suffice. Whenever treatment is considered useful and necessary, it needs to be aimed at the suspected underlying condition.
underlying condition. In clinical practice this mostly involves the prescription of antiepileptics, migraine prophylaxes, antiviral agents, or antibiotics. The literature indicates that antipsychotics are rarely prescribed and that in most cases their effectiveness is considered marginal. Moreover, when distortions are experienced as comorbid symptoms in patients with psychosis, it is important to take into account the possibility that they can sometimes be induced or aggravated by antipsychotics because of their potential to lower the threshold for epileptic activity (as has been described for risperidone).42

Limitations
The number of case descriptions of AIWS is small, especially considering the fact that the syndrome appears to be seriously underdiagnosed and that individual symptoms may be systematically neglected. This may be at least partly because international diagnostic classifications have so far refrained from including the syndrome. The operational definition of AIWS and its diagnostic criteria are in need of further development. More specifically, the question remains whether distortions in the olfactory, gustatory, auditory, sexual, coenesthetic, kinesesthetic, proprioceptive, algesic, vestibular, and thermic modalities should be added to the list of possible symptoms of AIWS. More importantly, however, the validity of AIWS as an independent nosologic construct needs to be assessed, as well as its overlap with related syndromes such as HPPD (which is also referred to in the literature as “LSD-induced Alice in Wonderland syndrome”).43 Other limitations are the lack of systematic epidemiologic data and our limited insight into the many etiologic and pathophysiological mechanisms possible in this context. Functional imaging techniques such as SPECT and fMRI have the potential to aid in localizing the network structures involved in mediating the symptoms of AIWS; however, so far, only 5 case reports have been published, probably because patients with longer-lasting distortions are hard to find and contrast signals in individual patients may be weak.

CONCLUSIONS
Since 1955, no more than 169 case descriptions of AIWS have been published. The literature indicates that this may be only the tip of the iceberg, with many individual symptoms of AIWS being experienced (albeit occasionally and only fleetingly) by up to 30% of adolescents in the general population. Although reassurance seems to suffice in roughly half of the clinical cases, the suspicion of a central origin of the symptoms should prompt auxiliary investigations in the form of blood tests, EEG, and brain MRI. Although firm evidence to justify these auxiliary investigations is lacking, I recommend them on clinical grounds because of the spectrum of known etiologies and the prospect of improved outcome in a substantial number of cases after adequate treatment. Treatment, if necessary, needs to be directed at the suspected underlying cause. Regarding research, much larger patient sample sizes are needed to allow for sufficient statistical power of empirical studies of AIWS and its individual symptoms. In addition, epidemiologic surveys in the population at large are needed to establish sound prevalence data. As an alternative or an adjuvant strategy, one might consider creating an international database for cases of AIWS, with special attention paid to phenomenological characteristics, diagnostic findings (including substance abuse), natural course, and treatment results. For such a database to be effective, all new cases of AIWS should be subjected to a systematic assessment, including proper history-taking, neurologic and other physical examinations, and auxiliary investigations.
In chronic cases, functional imaging techniques may be helpful in establishing specific neurobiological correlates of individual symptoms (although there are often various practical obstacles to be overcome). AIWS is in need of proper representation in international diagnostic classifications such as the ICD (for example under the heading of “Diseases of the Nervous System, Episodic and Paroxysmal Disorders” or “Other Disorders of the Nervous System”) and the DSM (preferably under a new heading called “Perceptual Disorders,” which in future editions might also include other nonpsychotic perceptual disorders such as the Charles Bonnet syndrome, exploding head syndrome, and cenesthesiopathy). Last but not least, our insight into the nature of AIWS might be enhanced by network analyses of the mutual relationships of individual symptoms as well as their relationships with the perceptual networks underlying them. In the meantime, however, it is possible to carry out a careful diagnostic procedure to help this partly hidden group of patients obtain a proper diagnosis and, if possible, adequate reassurance and, if necessary, appropriate treatment.

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Alice in Wonderland syndrome: A systematic review

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