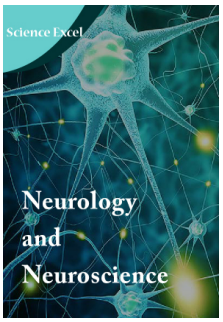
Neurology & Neuroscience

Case Report



Diabetes Insipidus And The Unsuspected Capacity Of Human Body To Dissociate The Water Molecule, Like Plants: Case Report

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Abstract

Central diabetes insipidus (CDI) is the result of several conditions that affect the hypothalamic-neurohypophysis system. Diabetes insipidus is a disease in which large volumes of dilute urine (polyuria) are excreted due to vasopressin (AVP) deficiency [central diabetes insipidus (CDI)]. These adipsic CDI patients are treated with desmopressin and adjusting the amount of daily water intake based on body weight measurement; but controlling the water balance is extremely difficult, and morbidity and mortality are shown to be high in these patients. However, the discovery of the intrinsic property of melanin to dissociate the water molecule marks a before and after in the diagnostic, study, and treatment of patients affected by Central diabetes insipidus.

Working on eumelanin has usually been regarded as an intriguing, though sometimes frustrating experience. The molecular mechanism by which eumelanin dissipates the radiation it absorbs was not known until we discovered it (water dissociation) in 2002, during an observational study that began in 1990 and ended in 2002. The working hypothesis was to try to correlate the anatomical characteristics of the blood vessels that enter and leave the optic nerve and the three main causes of blindness in the world. This study allowed us to identify the unsuspected capacity of the human body to transform the energy of sunlight into chemical energy, through the dissociation of the water molecule, as in plants.

Introduction

The posterior pituitary consists of magnocellular neurons that produce AVP and/or oxytocin. The cell bodies of magnocellular neurons are in the paraventricular and the supraoptic nuclei, and axons project to the neurohypophysis where the hormones are secreted into the blood stream. The blood supply for the anterior pituitary is via the hypothalamic-pituitary portal system from the suprahypophyseal arteries, the vascularization of the posterior pituitary is direct from the inferior hypophyseal arteries.

The maintenance of water balance in healthy humans is achieved principally by three interrelated determinants: thirst, AVP and kidney function. Apelin – a bioactive peptide – has been isolated from bovine stomach extracts (like ghrelin, another stomach-hypothalamus association). It is expressed in the supraoptic and paraventricular nuclei and exerts its action on specific receptors located on vasopressinergic neurons. Apelin acts as a potent diuretic neuropeptide which counteracts AVP actions through inhibition of AVP neuron activity and AVP release. The coexistence of apelin and AVP in magnocellular neurons, along with their converse biological effects and regulation, is likely to play a key role in maintaining body fluids [1].

AVP acts on its major target organ, the kidney, where it increases urine osmolality. It binds to the V2-receptors in the basolateral membrane of the renal collecting tubular and activates the Gs-adenyl cyclase system, increasing intracellular levels of cyclic 3′,5′-adenosine monophosphate (cAMP).

An increase in polyuria occurs when more than 80% of the AVP-secreting neurons are damaged. Extensive destruction can be caused by a variety of pathological processes including environment pollution causes. There is a selective loss of magnocellular neurons in the paraventricular nuclei with moderate gliosis and a relative preservation of small neurosecretory cells [2], suggesting that the disorder is due to degeneration of these hypothalamic neurons.

Around 20–50% of cases are considered 'idiopathic', the underlying process of pituitary stalk (PS) thickening in idiopathic CDI is not completely understood (primary hypophysitis?). Central diabetes insipidus (CDI) may be caused by vascular brain damage,

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but the pathophysiology of such a mechanism has never been precisely understood. In a group of patients with idiopathic CDI and normal anterior pituitary function, standard MRI showed a normal PS and AP gland size [3].

Dynamic MRI studies after contrast-medium injection revealed the absence of posterior pituitary lobe enhancement, whereas normal enhancement of the AP was present. The lack of contrast enhancement of the posterior lobe suggests that a selective vascular injury to the inferior hypophyseal arteries could be causally linked to CDI. CDI is the most frequent CNS manifestation of Langerhans Cell Histiocytosis (LCH), occurring in 10–50% of all patients [4].

Clinical examination may provide important clues to possible underlying diagnoses. The age at which symptoms develop together with the pattern of fluid intake, may influence subsequent investigation of diabetes insipidus. The primary symptoms are persistent polyuria and polydipsia, and young children may have severe dehydration, vomiting, constipation, fever, irritability, sleep disturbance, failure to thrive and growth retardation. Nocturia in children often presents as enuresis. Severe dehydration of early onset in males is highly suggestive of NDI; some mental retardation has been reported, probably caused by repeated and unrecognized dehydration before the diagnosis has been established.

Diagnosis of CDI is based on the demonstration of plasma hyperosmolality (> 300 mosm/l) associated with urine hypoosmolality (< 300 mosm/l or urine/plasma osmolality ratio < 1) and polyuria (urinary volume > 4–5 ml/kg/h). In an MRI, the posterior pituitary can be seen as a hyperintense signal on sagittal T1-weighted imaging under basal conditions. A lack of posterior pituitary hyperintensity (although not specific), is a hallmark of hypothalamic-posterior pituitary disorders and may signify the early stage of occult local tumors. Multiple pituitary hormone deficits were present in 30– 50% of patients with a widened pituitary stalk (PS) while only 10% of the 19 patients with normal PS had an additional hormonal deficit [5].

Although little is known about how the brain orchestrates systemic osmoregulation, recent advances have been made in our understanding of the molecular, cellular and network mechanisms that mediate the central control of osmotic homeostasis in mammals [6].

The drug of choice for the treatment of diabetes insipidus is DDAVP, a synthetic analog of the endogenous hormone arginine AVP, but with a 2,000- to 3,000-fold lower vasopressor effect. DDAVP may be administered orally, intranasally, or parenterally. Given intranasally or orally, maximum plasma concentrations are reached in 40–55 min. The drug's half-life is 3.5 h. Generally, urine output will decrease 1 or 2 h after administration and the duration of action will range from 6 to 18 h. There is broad individual variation in the dosage required to control diuresis. Symptomatic dilutional hyponatremia is the only potential hazard if DDAVP is administered in excess over a long period of time. Symptoms of hyponatremia include headache, nausea, vomiting and seizure.

Rare side effects with intranasal delivery of DDAVP include eye irritation, headache, dizziness, rhinitis, or epistaxis, coughing, flushing, nausea, vomiting, abdominal pain, chest pain, palpitations, and tachycardia [7]. But these adipsic CDI patients, despite to be treated with desmopressin and adjusting the amount of daily water intake based on body weight measurement; the control of the water balance is extremely difficult, and morbidity and mortality are shown to be high in these patients. A high prevalence of treatment-associated side-effects, mismanagement during hospitalization, and psychological comorbidities, are reported [8].

Central diabetes insipidus and the oxygen, hydrogen, and high energy electrons

The detailed descriptions that have been published to date about the CDI, the findings described, both anatomically and functionally [9], are more compatible with a generalized failure than with a punctual lesion. And widespread failures, in any system, are markers of problems in the power supply.

The CNS structures that are affected (Neuro-hypophysitis) and give rise to central diabetes insipidus (CDI) require, like any cell, tissue, organ, and system, a constant, relentless supply of oxygen, hydrogen, and high-energy electrons to function properly, just as it has happened over millions of years, since the beginning of time.

To-date melanins fundamental structure is still under intense scrutiny [10]. Melanin consists of a very high molecular weight polymer made up of different units in various oxidation states and linked randomly [11]. Scanning electron microscopy (SEM) investigations of the morphology of melanins show that they are amorphous solids even at the micrometer scale [12].

The optical and photophysical properties of eumelanin are rather unique and have been comprehensively reviewed by Meredith and Sarna, although none of the models proposed to date provides a complete and fully satisfactory explanation of eumelanin properties. It is likely that the difference between our results and those of other researchers is because we studied melanin in one of its natural locations: the retinal pigmented epithelium and the choroid of the eye. It is said that melanin resists the laboratory methods available to date.

Case Report

Male patient, born in 2000, dedicated to the cultivation of ornamental plants in Villa Guerrero, in the state of Mexico, México, who, in September 2020, he began to drink a lot of water, up to 10 liters a day. At the beginning of the disease, he lost 15 kg in a month, thereby, he was hospitalized several times due to severe dehydration, and after several weeks and diverse studies the Dx was reached: Central Diabetes insipidus (CDI). He was prescribed DDAVP Tablets under the tongue and spray in the nose, but after few days they are no longer working and the DDAVP produced severe irritation of the nasal mucosa at the application site, which even led to local bleeding. Doctors told him that he had a small tumor.

He went to the consultation referring to feeling very tired and with marked polydipsia of up to 10 liters of water every 24 hours.

Of the studies that the patient brings with him on the day of the first consultation, we have the following:

Hyperuricemia 8.9 mg/dL, elevated phosphorus 5.3 mg/dL, polyglobulia 17.5 g %, normal serum cortisol 17.2 µg/dL, glycosylated HB (Hb-A1c) 5.5%, normal thyroid profile, hepatic USG reports 11 mm vena cava, 4 mm common bile duct, normal urinary electrolytes, plasma creatinine 0.9 mg %, Creatinine clearance 63.1 ml/min; serum osmolarity 294 to 296, urinary density 1015, urinary osmolarity 525, Electrocardiogram shows sinus arrhythmia, sinus bradycardia 50 to 60 x minute. Renal USG shows bilateral, non-specific chronic inflammatory process.

MRI Images

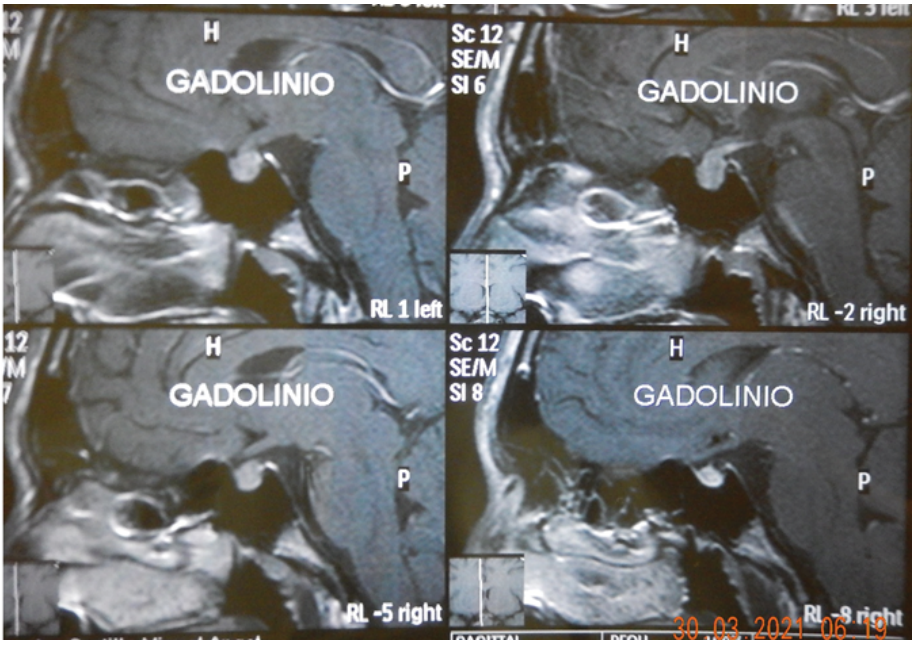

Figure 1. *Widening of the pituitary stalk.*

Figure 2. *Optic nerve and macular region of the right eye. The appearance is normal, only discrete pseudo-fluorescence can be seen in the region of the optic nerve excavation.*

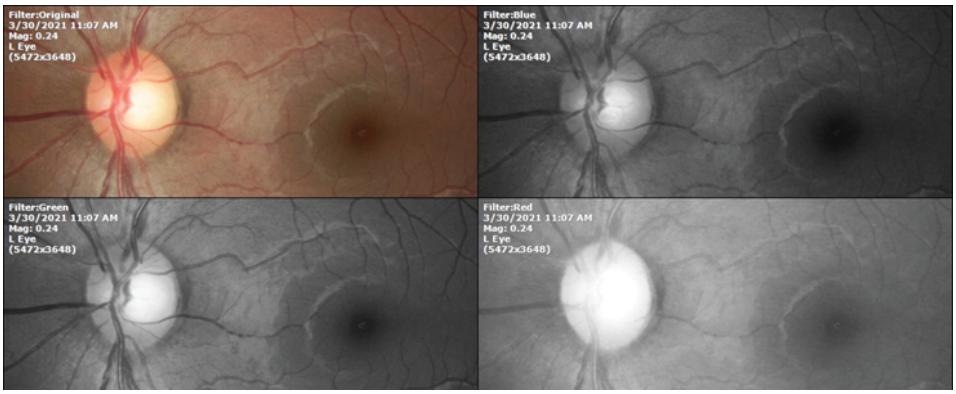

Figure 3. *In the fundus examination on the left side, only moderate pseudo fluorescence is seen in the optic disc excavation..*

Given the patient's history of chronic occupational exposure to agrochemical agents, such as pesticides, herbicides, and fertilizers, and the lack of response to nasal and sublingual DDAVP, we agreed with the diagnosis of central diabetes insipidus (CDI), compatible with the magnetic resonance image that demonstrated dilation of the pituitary stalk, but according to our experience, contamination of water, air, and food with agrochemicals can cause almost any clinical picture, so the patient was explained the possibility after being treated with QIAPI 1®, to restore the accuracy of reaction of water dissociation that happens inside neuromelanin and is lost when exposed to agrochemicals, which was accepted by the patient and his relatives. The recommended dose was three drops under the tongue every hour, all the time he was awake. The DDAVP application was suspended.

Six months later, on September 30, 2021, the patient returned for a follow-up consultation, referring to feeling better, and he is already drinking the normal amount of water. He reports mild, occasional headaches, but in general he feels much better, and he has already regained the weight he had lost. He refers that 20 days after treatment he began to notice improvement.

Before our treatment, if he didn't drink water, he would dehydrate very quickly, in a matter of a few hours. The ophthalmological examination shown:

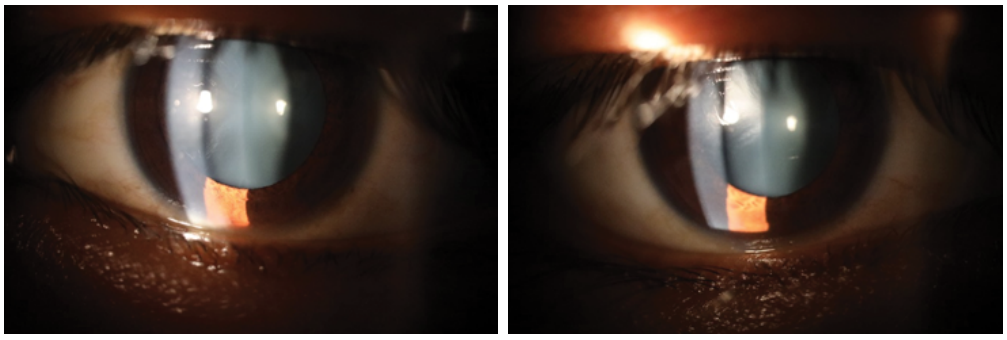

Figure 4. *Photographs of the anterior segment of the right side (left) and of the left eye (right), where the integrity of the structures can be seen.*

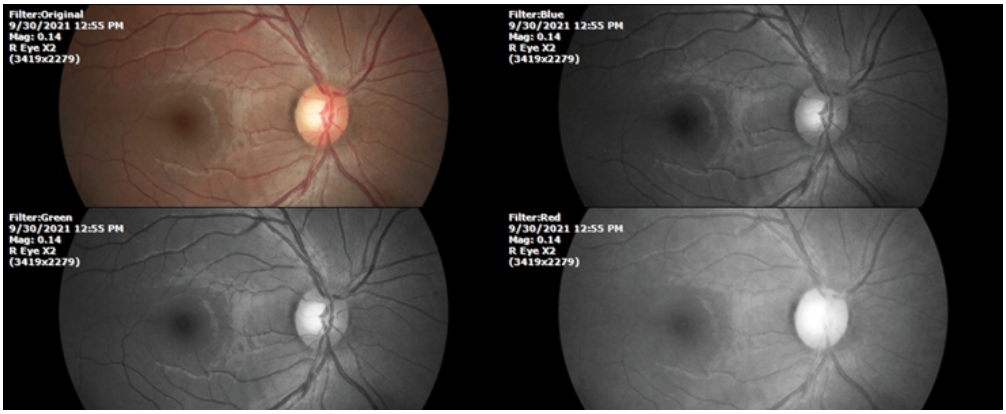

Figure 5. *In the ophthalmoscopic examination of the right eye, no significant differences were observed in relation to the first examination carried out on March 30, 2021, perhaps the pseudo fluorescence of the optic nerve excavation has decreased slightly.*

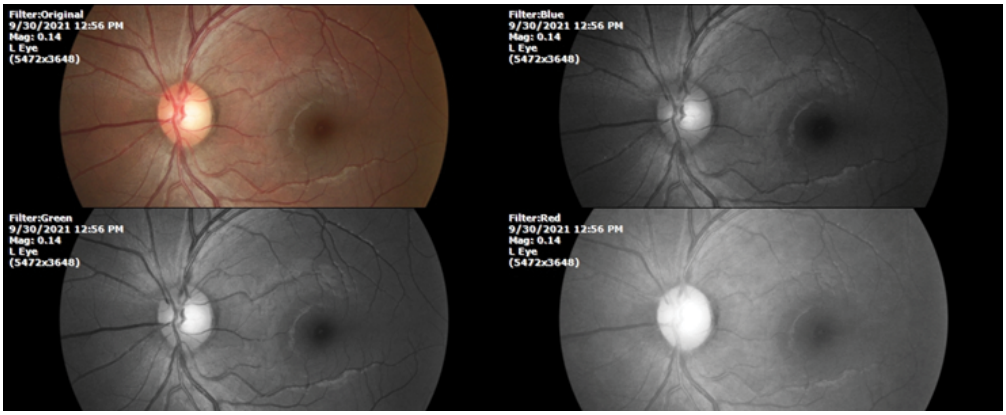

Figure 6. *The assessment of the structures of the left eye fundus did not show notable changes in relation to the initial ophthalmoscopic examination carried out on March 30, 2021.*

Figure 7. *The clinical appearance of the former patient is very satisfactory, he has no longer had symptoms, the weight he regained has remained stable. It was recommended to continue with the treatment and go for a new evaluation in a year.*

Given the notable symptomatic improvement, the patient was suggested to continue with the same treatment and return in six months for a new evaluation. The ophthalmological examination continued without change and we only show the patient's clinical photograph, where the remarkable recovery of what we can label as central diabetes insipidus caused by agrochemicals can be seen. We consider central diabetes insipidus to be a chemical disease.

Comments

Our observation that our body does not take oxygen from the air that surrounds it, but from the water it contains inside the cells that make it up [13], has been a disruptive discovery, since the clinical results of our therapeutic approach support the validity of our initial observation, which was not the product of chance, but was the result of an observational, descriptive study, in which our working hypothesis was to study the possible correlation between the blood vessels that enter and leave the optic nerve and the three main causes of blindness in the world, namely: macular degeneration, diabetic retinopathy, and glaucoma.

Said study began in 1990 and ended in 2002 and included the ophthalmological studies of 6000 patients. But the effort was worth it, since it allowed us to identify a chemical reaction that at that time was only known in plants: the dissociation of water, that is: the transformation of the power of sunlight into a type of chemical energy capable of being used by living beings. Apparently the almost universal mechanism used by nature is through the dissociation of the water molecule, because through this reaction, the eukaryotic cell obtains the oxygen, hydrogen, and electrons it requires to drive and therefore carry out the myriad intracellular chemical reactions that make up life [14].

In the case of the central nervous system, a paradigm is also broken and a new one is created, as it turns out that the main source of oxygen for the CNS is not the oxygen of the atmosphere that surrounds us, but rather that the main source of oxygen is neuromelanin, located mainly in the substantia nigra, the locus coeruleus, and to some extent in the meninges.

The dissociation of the water molecule that occurs inside neuromelanin is an exact, amazingly exact process that has not changed since the beginning of time, since it constitutes the initial spark of life in both plants and animals. But said accuracy is disturbed by polluted water, polluted air, pesticides, herbicides, fertilizers, metals, plastics, solvents, industrial waste, soft drink additives, fast food, alcohol, etc. extreme temperatures etc.

So, the levels of oxygen, hydrogen, and electrons that the cell obtains by constantly dissociating the water molecule through the melanin granules that all eukaryotic cells contain, are very strict, their tolerance margin is very narrow because the fundamental processes of the cell are incessant, so that when the very first reaction of life (the dissociation of water) becomes unbalanced, the harmony of the whole is affected and then some symptom or disease may appear.

We are at the beginning of a new era in biology and therefore in medicine, since the concepts we have about molecular biology require rewriting, rethinking, and reorganizing.

Acknowledgements

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QIAPI 1™ was developed at our facilities.

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