(REVIEW ARTICLE)

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Heavy metals, halogens, carbon and nitrogen oxides, and autism the important role of digital technologies in health education, prevention and digital health

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Abstract

In recent years, neurodevelopmental disorders have been increasing. This article analyzes one of the causes causing the specific disorders. Through a literature review will be examined the environmental factors that are considered one of the causes of autism. In particular, the negative effect of heavy metals and other harmful elements in the atmosphere will be reported.

Keywords: Autism; Heavy metals; Halogens; Environmental pollution; Cancer

1. Introduction

Neurodevelopmental disorders such as autism, attention deficit disorder, mental retardation, and cerebral palsy affect large proportion of children in the US (Landrigan et al, 2012). The factors that cause autism are trying to be understood. People with autism present social problems. Of course, they may also have additional comorbidities such as learning and cognitive difficulties, anxiety, low intelligence, behavioral problems, and many others (Sulaiman, Wang & Ren, 2020).

The alarming increase in the incidence of autism disorder has led many scientists to study its causes. It is argued that neurodevelopmental disorders are caused by genetic and environmental factors, which both work together to cause or worsen these disorders (Kaur et al, 2021) [18]. A USA study estimated that 25% of developmental disabilities are the result of the interaction of environmental and genetic factors (National Research Council, 2000).

Unfortunately, little importance is given to the role of the environment, although it is very important since we live and breathe in it. The atmosphere contains a variety of elements, some of which can cause changes in the body. For example, the exposure of the human body to heavy metals seems to be linked to the disorder of autism as they also play a negative role in the nervous processes of the brain. Some effects of minerals are the occurrence of oxidative stress, dysregulation of glutathione, cell dysfunction, and autoimmune diseases (Kaur et al, 2021) [18]. The toxic effect of metals in combination with an inadequate diet increases the severity of symptoms (Blaurock-Busch et al, 2012) [5].

Heavy metals are classified as neurodevelopmental toxins because they appear to cause additional fetal damage leading to neurological defects (Gorini et al, 2014) [15]. In addition, developmental vulnerability can also occur during infancy and childhood due to brain development at these ages (Rodier, 1995) [27].

The daily exposure of our bodies to heavy metals is unavoidable. Knowing the effects can initially put our body in a detoxification process by reducing its exposure to the specific metals by avoiding substances that include them. Secondly, we can strengthen our body and shield it from heavy metals by strengthening our immune system. This can

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be achieved by taking vitamins, such as vitamins C and E, and trace elements, such as zinc and selenium (Kaur et al, 2021) [18].

It would be appropriate, therefore, to study each metal separately and the other elements that cause environmental pollution.

2. Heavy metals

2.1. Mercury Hg

One of the leading environmental pollutants worldwide is mercury which appears to be directly related to the development of autism spectrum disorder symptoms. Research has shown increased amounts of mercury in the hair, teeth, urine, and blood of patients with autism. Mercury can be transferred through the placenta to the fetus and becomes dangerous for pregnant women who exposed to this toxic metal. Cognitive problems were observed due to organelle destruction and immunoglobulin accumulation in the brain (Kaur et al, 2021) [18].

Mercury is found in the natural environment and is mostly released during industrial activities. Dental amalgams, medicines and industrial products contain mercury, which can cause permanent damage to the central nervous system. References have also been made to the existence of mercury in vaccine preservatives, which, however, is easily excreted by the organism and may not cause health problems. Variety of studies reported very high amounts of mercury in children with ASD compared to the control group. Neuromuscular, sensory and memory problems also appeared in these children. (Sulaiman, Wang & Ren, 2020) [32].

Because of effects of mercury many industrialized countries have established strategies to minimize mercury exposure. Inhalation of mercury passes the blood-brain barrier and from the lungs ends up in the central nervous system. Gorini et al (2014) [15] report that mercury poisoning and autism present similar physical and mental symptoms. Collectively, many studies point to mercury as a causative factor in autism. Higher levels of mercury in the hair and urine of children with autism indicate greater exposure to mercury in the past.

2.2. Aluminum Al

Aluminum is among the environmental metal components that are blamed for the faster onset of autism symptoms. This is explained by the fact that when the specific element enters the body, the action of an enzyme is affected, resulting in the malfunction of glycolysis, a process necessary for energy in brain mechanisms. In addition, the imbalance of homeostasis in the brain is created. But where can this toxic element be found in our daily life? Aluminum is found in cookware, aluminum foil, cans, antiperspirants, building materials, and many forms of transportation. Research has also reported on the existence of arsenic in vaccine substances to optimize their effectiveness (Kaur et al, 2021) [18].

Aluminum can also be found in medicines, parenteral nutrition given to patients, cosmetics, and industrial products. Most dangerously, it is found in most drinking water, whether bottled or tap water. Many organizations have set an upper limit for ingestion, exposure, or inhalation of this metal because characterized by various agencies as a very hazardous substance. It is important to mention that aluminum crosses the placenta and can be transferred to breast milk. Sulaiman, Wang & Ren's 2020 [32] research on people with autism reported high aluminum content in all areas of their brains. This event can cause encephalopathy, dementia, and reduced cognitive function.

Regarding aluminum and autism, research shows that they are related. More specifically, the aluminum that you include as an adjuvant in some vaccines has been blamed for the onset of autism. For this reason, health surveillance is required to detect adverse effects of vaccines. On the one hand, adjuvants multiply the reactivity of vaccines, but on the other hand, their toxicity also multiplies. Boretti's 2021 [7] study was based on three lines of evidence that aluminum is associated with this particular disorder. Ecological studies, animal studies, and measurements of aluminum in the brains of children with ASD suggest a neurotoxic link between this particular toxic metal and autism.

2.3. Arsenic As

As mentioned above, a main pathogenic factor in the occurrence of autism spectrum disorders are the environmental factors which are include the above heavy metals as well as arsenic. A recent study in Poland evaluated hair samples from 30 children with ASD and 30 children without ASD. The results of the analyzed data showed that calcium in children with autism was lower than other children and also that arsenic was statistically significantly higher in these children. In conclusion, children with ASD suffer from toxic metal overload, which may play a major role in the pathogenesis of autism (Filton, 2020) [13].

Arsenic is found in various Asian and American countries. It occurs in many forms like as salts and is mostly used in the field of industry. Contamination of drinking water by arsenic is frequently observed and its consumption appears to cause alterations in the brain resulting in increased oxidative stress, memory loss, psychiatric and cognitive problems. It is important to mention that a variety of studies have studied arsenic exposure in typical children and children with autism. The group of autistic children was found to have higher amounts of arsenic in the body (Kaur et al, 2021) [18].

The multidisciplinary study by Tripathi et al (2022) [33] referred to earlier research that has already demonstrated that exposure to arsenic leads to the development of several neurological disorders. Behavioral studies have shown cognitive impairments similar to those of autism spectrum and Alzheimer's disease. Also, genetic mutations are considered relevant to the environmental neurotoxicity of arsenic. It is very important to mention that this particular heavy metal affects the hippocampus and behavioral effects have been reported.

2.4. Lead Pb

Another important toxic metal is lead which, in combination with arsenic and aluminum, leads to neurodevelopmental problems. Lead can be found in water and in food which can make it extremely dangerous to health. Of course, this metal is also found in other sources of everyday life, such as in cars and aircraft, paints and toys. In fact, elevated levels of lead in the blood affect the antioxidant activity of vitamin E and glutathione, as well as creating learning and memory problems. Dysfunction of the blood-brain barrier appears to be induced following lead exposure resulting in oxidative stress (Kaur et al, 2021) [18].

Lead poisoning can even cause death. The cases of children who survived poisoning presented with cognitive and behavioral problems, difficulties with concentration and memory, problems with IQ and ADHD. They also manifested problems in communication and speech, symptoms that suggest a relationship with the onset of autism. In urban areas lead concentration levels can reach very high levels. The easy absorption of lead from the gastrointestinal tract of children is estimated to be due to the main sources of this toxic metal being the burning of gasoline and the use of paints during home renovation. Additional sources of lead are soil and dust in drinking water, toy paint, ceramic glass, and electronic waste (Gorini et al, 2014) [15].

From all the above it follows that the neurotoxicity of lead affects the mechanisms of action. Lidsky & Schneider 2003 [21] state that these mechanisms include disruption of calcium homeostasis, mitochondrial damage, mitochondrial calcium release, altered lipid metabolism, astrocyte accumulation, and thyroid hormone transport into the brain. Damage to the latter mechanism is critical because it delays the normal development of the brain and can cause mental retardation.

2.5. Cadmium Cd

In 2010, the danger of cadmium, a neurotoxic metal that can be found in the soil, the food chain, and cigarette smoke, was highlighted. Cadmium has been linked with neurodegenerative diseases such as Alzheimer's. It can also cause chromosomal damage and inhibit cell growth (Sulaiman, Wang & Ren, 2020) [32].

Cadmium is emitted from industrial and agricultural sources and is considered one of the most dangerous environmental substances along with lead and mercury. This metal is easily detectable in fish, meat, and vegetables. Through the consumption of these foods, cadmium accumulates in the liver and nerves. Even low-dose cadmium accumulation was associated with reduced IQ in children. Also, urinary concentrations were associated with an increased risk of learning disabilities. On the other hand, increased levels of cadmium in hair showed social problems and deficits in children (Gorini, 2014) [15].

Further research has shown that exposure to cadmium causes oxidative stress by affecting antioxidant proteins. It means that glutathione and metallothionein are affected in turn, resulting in the reduction of cells. Cadmium exposure has also been associated with prostate and lung cancer, kidney failure, bone disorders, and DNA damage (Bertin & Averbeck, 2006) [4].

2.6. Antimony An

Diagnoses of metal poisoning can be made from urine, blood and hair. So, Blaurock-Busch et al in 2012 [5] conducted a research. They analyzed hair to detect the presence of metals. The participants were 44 children with autism aged 3 to 9 years. The results proved that the the antimony was high in children with autism. This fact increases the symptomatology in combination with nutritional deficiency.

In one region of Saudi Arabia, a study was conducted involving 77 autistic children in which heavy metals, including antimony, were measured. The main results were that children with ASD characterized by significantly higher levels of metals such as antimony and lower levels of trace elements. Comorbidity with other disorders - such as difficulties in sleeping, speaking and eating - was observed in these children. Also in areas where elevated levels of antimony were found in the water, fetal and infant mortality was observed, with attention deficit disorders and reduced mental capacity. Apart from water, the specific metal can be absorbed into dental materials too (Al-Ayadhi, 2005) [2].

The study by Adams et al (2009) investigated the relationship of autism symptoms to toxicity in the body. One of the metals with the greatest negative effect was antimony, which causes oxidative stress and thiol reduction. On the one hand, these are two causal roles in creating autism symptoms. On the other hand, the increase in oxidative stress and the decrease in thiol may enable the individual to accumulate a greater amount of antimony and other metals.

2.7. Chromium Cr

The study by McDermott et al (2015) [23] focused on the effect of toxic forms of chromium during pregnancy and the effects on children. Ten pregnant women and their children were examined. Two of the studies that included chromium linked the heavy metal to lymphocyte damage in the fetus. The next three studies showed effects on DNA and the onset of autism.

In general, chromium is one of the most common toxic metals that can be detected in the hair of people with autism. In fact, exposure to chromium in combination with the lack of basic nutrients such as iron and calcium play a causal role in the etiology of autistic disorders. Also, elevated chromium levels are associated with poor verbal communication, impaired taste and smell (Blaurock-Busch et al, 2012) [5].

The harmful effects of heavy metals on the body are well known. Yorbik in 2010 [35] investigated the levels of heavy metals in the urine of children with autism and healthy individuals. Urine chromium levels were significantly elevated in all 30 children with autism. This can cause oxidative stress which is linked to autism, because antioxidant enzyme activities are lower in children with autism. Finally, increased levels of chromium in the body may contribute to decreased levels of cysteine and glutathione.

2.8. Nickel Ni

The same research by Blaurock-Busch et al in 2012 [5] also shows that high nickel levels are associated with fear, nervousness, and reduced non-verbal communication. Nickel affects the absorption of trace elements and can also interact negatively with other essential minerals for the body such as iron. In this way, the nervous system is affected and there may be damage to cognitive development.

McDermott et al in 2015 [23]also looked at the effect of nickel before and during pregnancy. The results showed that some of the studies linked nickel with preterm birth. Also, a small correlation appeared to have the toxic metal with the birth weight of the babies. In addition, birth defects appeared to be present in newborns when pregnant mothers were exposed to nickel. That is, a group of babies showed musculoskeletal as well as cardiovascular defects, problems in the nervous system, and malformations of genital organs. Finally, most of the research linked nickel - along with chromium, as mentioned above - to autism.

Heavy metals including nickel can be detected in the air making it easier to be poisoned by exposure to them. Metal poisoning is one of the most common environmental disorders. Nickel is considered very toxic and causes a negative reaction in the immune system. The main sources of nickel are dental cases and jewelry (Al-Ayadhi, 2005) [2].

2.9. Cuprum Cu

Industrialization and urbanization have led to the release of all of the above highly toxic heavy metals, resulting in the contamination of water and wastewater. Of course, metals of lower toxicity such as copper also contribute to this contamination. In previous years it was observed that medicines, detergents, preservatives, and others had effects on the environment. With the amounts of industrial waste ending up on the ground, an ecological imbalance is caused resulting in the accumulation of metals. In this way, the drinking water consumed by humans is also contaminated and its oxidative stress is triggered (Mathew et al, 2016) [22].

There also appears to be a correlation between copper concentrations and autism. More specifically, based on the information collected from articles, the concentration of hair, nail and blood samples was evaluated and it was found

that the concentration of copper and autism is not very related. More important was the relationship of the disorder with other metals and less with copper (Mohammadabadi et al, 2020) [24].

In conclusion, heavy metal poisoning is a common health problem. Heavy metals can become harmful to health. Copper also causes oxidative stress by creating free radicals and reducing antioxidant levels. It also alters DNA and inhibits its function (Kim et al, 2019) [19].

3. Halogens

3.1. Fluoride

Fluoride is an additional element being investigated. A serious worldwide problem is water contamination due to which a large population including many children have fluoridation. Fluoride in water and soil can come from minerals (geogenic source) but it can also come from industry, the use of fertilizers (anthropogenic source). Thus, when drinking water or food containing fluoride, it enters the human body and causes health problems. Excess fluoride can lead to dental and skeletal fluoride. Chronic consumption can cause bone deterioration, impaired cognition, impaired intelligence, and developmental problems. Ingested fluoride is rapidly absorbed through the gastrointestinal tract and lungs (Yadav, 2018) [34].

Research by Choi et al (2017) [10] reports in their review of published studies on the neurotoxicity of fluoride causing problems in neurobehavioral development. The results of the meta-analysis prove the possibility of a negative effect on high amounts of fluoride, since the children exposed to them presented a lower IQ than the rest. Dental fluoridation is a major indicator of high fluoride consumption.

Fluoride can cause metabolic disorders. Autistic individuals are observed to have higher amounts of fluoride. Fluoride causes symptoms seen in people with ASD such as mitochondrial dysfunction and energy depletion, oxidative stress, and inflammation. More generally, heavy metals in combination with organic pollutants and endocrine disruptors contribute to the pathogenesis of ASD and cause, in addition to the above, alterations in neurotransmitters (Strunecka & Strunecky, 2019) [31].

3.2. Chlorine

The presence of pathogens in contaminated water is one of the main causes of waterborne diseases, such as hepatitis and bacterial gastroenteritis. For this reason, efforts are being made in Saudi Arabia to improve water distribution systems in order to minimize the risk to human health (Sharif, 2017) [29].

But chlorine is a mineral used in water as a disinfectant and has been accused of adversely affecting human health. Either inhalation of chlorine or dermal exposure to it is of concern. On the one hand, chlorine has oxidizing properties, killing harmful microorganisms. Chlorine can also be used as a bleaching agent. Also, in contact with organic materials it releases some compounds that are considered to be related to brain cancer and problems of the immune and reproductive system (Drogui, 2015) [11].

Finally, chlorine intake has also been blamed for the appearance of hypertension and blood pressure (He, et al, 2022) [17].

3.3. Bromine

Bromine is used extensively in food and the soil in which food is grown. Many methods have been developed over time to detect bromine in foods in order to prevent their consumption (Getzendaner, 1975) [14].

More specifically the study by Ventura et al (2018) [36] tries to give an overview of the risk of bromine. Fruits, fish and vegetables are important groups of nutrients necessary for the good health of the body, so their daily consumption is recommended. Nevertheless, references are also made to the toxic effects of specific foods due to the existence of toxic elements. Pollution can affect the quality of food so it can be considered dangerous for health.

This is because research findings indicate that in addition to heavy metals, the risk of developing autism increases after prenatal exposure to halogens or pesticides. The risk becomes even greater when infants are subsequently exposed to chemicals such as bromine. In this version, there can also be a comorbid intellectual disability. Certainly the risk

becomes more intense the younger the child is and more specifically during the first year of life. So neurodevelopmental disorder is likely to occur when someone is exposed to bromine (Ehrenstein et al, 2019) [12].

3.4. Iodine

Iodine is another element in the halogen group. It is considered a basic element for the human body, however in large amounts or its lack can create problems. Some of these are thyroiditis and mental illness. In many countries methods have been discovered to control daily intake through transformation since it can become toxic (Bhagat, et al, 2009) [6].

Iodine deficiency in pregnancy leads to hypothyroidism and impaired neurobehavioral development of the infant. In addition, too much iodine causes toxicity. Excess of this element can result from overconsumption of salt, water, and milk and leads to acute and chronic toxicity (Southern & Jwayyed, 2023) [30].

The article by Pennington (1990) [26] confirms the above results regarding the adverse effects of excessive iodine exposure. Excessive levels of iodine can also occur through the consumption of nutritional supplements or drugs or from tests that have x-rays. Very serious are the cases of mothers who receive more iodine than allowed and thus through breastfeeding it can pass to the infant, so it is necessary special attention.

4. Carbon monoxide and dioxide

The human body's exposure to indoor household pollutants is very important since people spend most of their time in closed spaces such as the home. These pollutants include particles, microorganisms and toxins. All these have a great impact on the health of children and adults, causing chronic diseases and increasing mortality. It is important to mention that household pollutants arise from cooking and household dust and release carbon monoxide that quickly passes through the bloodstream (Rosário, 2021) [28].

Carbon monoxide and lead are suspended in the air as so-called "smog". Carbon monoxide is emitted from cigarettes and is also present in the small dust particles that are easy to penetrate into the lower respiratory tract. As they enter the lungs and are transported through the blood circulation in the body, there we speak of toxicity (Grzywa-Celińska et al, 2020) [16].

Air pollution is a global environmental issue. Accumulating evidence from Annavarapu & Kathi's 2016 [3] research shows that urban air pollution can have a significant effect on the brain's central nervous system. Children exposed to air pollutants are vulnerable to behavioral disorders. Reducing fuel emissions and therefore carbon monoxide can improve air quality and therefore reduce the negative effects caused by air pollution.

5. Nitrogen monoxide and dioxide

In the same research (Annavarapu & Kathi, 2016) [3] the reference to nitrogen dioxide emissions seems to cognitive disorders in children. They also lead to oxidative stress, neurodegeneration, neurodysfunction, attention deficit and autism symptoms. The research reports that air pollution in external and internal environments has adverse effects on the cognitive development of the child.

Research in Mexico has identified potential links between air pollution, brain damage, and delayed cognitive development. Clinically healthy children without evidence of neurological disorder showed problems in cognitive function, memory, and executive functions (Calderon-Garciduenas, et al, 2008) [8].

In addition to the above, exposure to nitrogen dioxide greatly burdens health and can also cause premature birth, lung cancer, diabetes, and lung diseases (Chen, 2022) [9].

6. The role of digital technologies in healthy living Education and prevention

The digital technologies play an important role both in general education and in healthy living education and training for prevention as well as for intervention and rehabilitation. According to WHO a global strategy on digital health should encourage healthy lifestyles and wellbeing for people of all ages, everywhere. National or regional digital health projects must be directed by a solid strategy that combines organizational, financial, human, and technology resources if they are to fulfill their promise.

According to U.S.F.D.A. the broad definition of digital health encompasses fields like wearable technology, telehealth and telemedicine, personalized medicine, and mobile health (mHealth). Digital technology has been driving a revolution in health care, from artificial intelligence and machine learning to mobile medical apps and software that assist the clinical decisions clinicians make every day. The use of digital health tools has the potential to significantly improve individual patient care by enhancing the accurate diagnosis and treatment of disease. Computing platforms, networking, software, and sensors are all used by digital health technologies in the healthcare industry and other applications. These technologies have a wide range of applications, from uses in general wellness to uses as medical equipment. They comprise technologies created with the intention of being used as medical products, in medical products, as auxiliary diagnostics, or as companions to other medical products (devices, medications, and biologics). Additionally, they could be utilized to research or develop medicinal items.

Based on the views of European Commission, digital health and care refers to devices and services that make better use of information and communication technologies (ICTs) in order to monitor and control unhealthy lifestyle choices as well as to better prevent, diagnose, treat, and manage health-related concerns. Innovative digital health and care can increase access to treatment, raise the standard of care, and boost the industry's overall effectiveness. One of the six political priorities of the Commission for the years 2019 to 2024 is "A Europe fit for the digital age." The digital transition should be something that benefits everyone, putting people first and creating new opportunities for business, building on antecedent measures enhancing the formation of a Digital Single Market. Given the potential advantages that digital services may have for consumers and businesses in this sector, health is one of the industries covered by this agenda, and is described by 3 pillars-priorities.

6.1. Pillar 1: Safe access to and sharing of data

The Commission is developing the eHealth Digital Service Infrastructure to enable the sharing of e-prescriptions and patient summaries between healthcare providers in order to increase access to cross-border healthcare. The first cross-border transactions began in 2019 with the intention of bringing all other EU nations on board by 2025. The Commission is aiming to create a European electronic health record exchange standard that will eventually be available to all EU citizens.

6.2. Pillar 2: Connecting and sharing health data for research, faster diagnosis and improved health

The second pillar of the 2018 Communication is to take advantage of the enormous potential of health data to promote medical research with the goal of enhancing medical devices, medications, and treatments as well as prevention, diagnosis, and therapy.

6.3. Pillar 3: Improving individual care and citizen empowerment through digital services

Digital services have the potential to empower people, enabling them to take on more responsibility for managing their own health, from adhering to prevention guidelines and being inspired to live better lifestyles to managing chronic diseases and giving feedback to healthcare providers. Innovative care models that leverage telehealth and mHealth to address the growing healthcare demand will also be beneficial to health systems, assisting in the shift towards integrated and individualized care systems.

Last but not least, we emphasize the significance of all digital technologies in the field of healthy living education, which is very effective, productive, facilitates and improves the assessment, the intervention, and the educational procedures via mobile devices that bring educational activities anywhere [37-38], various ICTs applications that are the main supporters of education [39-46], AI, STEM, and ROBOTICS that raise educational procedures to new performance levers [47-50] and mobiles [51]. Additionally, the improvement and blending of ICTs with theories and models of metacognition, mindfulness, meditation, and emotional intelligence cultivation [52-63], accelerates and improves more the educational practices and results, especially in training parents and teachers in recognizing the sources of the environmental toxins for protecting the children and preventing them to exposed in the negative consequences of these toxins.

7. Conclusion

In the particular bibliographic article, heavy metals and atmospheric elements were associated with the onset of autism. Heavy metals exist in our daily life as in food, utensils, and toys. Therefore, the contact of the human body with metals such as lead, cadmium, chromium, and many others is frequent and dangerous. Long-term and continuous exposure to toxic metals creates neurodegenerative diseases, reduced IQ, attention deficit disorders, and reduced mental capacity. They can also cause oxidative stress, impairments in cognitive development, musculoskeletal and cardiovascular

problems, damage to the nervous system, and malformations of genetic organs. The above proves the toxicity and danger of metals.

Another important finding of the study was that air pollution may be associated with autism symptoms. More specifically, nitrogen and carbon monoxide, and dioxide are present in the atmosphere. Emissions in them have indications of neurological disorders, and problems in cognitive function, memory, and executive functions. They also cause diseases such as diabetes, cancer, and lung disease. An additional finding that should be mentioned are the halogens, such as fluorine and chlorine, which are among the toxic elements and cause diseases and autism.

In summary, the findings of this study contribute to the research literature investigating heavy metals, halogens, and air pollution elements in relation to the occurrence of autism and various diseases. The fact that environmental factors blamed for neurodevelopmental disorders should be the subject of future research to better address disorders as well as diseases.

Compliance with ethical standards

Disclosure of conflict of interest

The Authors proclaim no conflict of interest.

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