

A Novel Hybrid Approach to Children with Autism Spectrum Disorders

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Abstract

Objective: The objective of our research and this paper is to provide a sufficient treatment, mainly symptomatic, of autism spectrum disorders which remain terra incognita to contemporary neural science.

Approach: In our experiment, we used the 'cavity structure effect' and the pharmacological effects of plant-derived metabolites to stimulate and 'functionally correct', as much as possible, the nerve system of children up to 7 years of age, diagnosed with autistic disorders.

Main results: Under the beneficial impact of the above-mentioned physical and chemical phenomena, an improvement in the overall performance of the examined patients was observed.

Significance: This paper should serve as an initial theoretical and, to a certain extent, practical basis for more extensive research and appropriately designed clinical studies.

Keywords: Autism; Cavity structure effect; Farnesol; Syringa vulgaris; Synergin; Quantum vortex ring

Abbreviations: APA: American Psychiatric Association; ATEC: Autism Treatment Evaluation Checklist; ASD: Autism Spectrum Disorders; BAS: Biologically Active Substances; CS: Cavity Structures; CSE: Cavity Structure Effect, Cavernous Structure Effect; DSM: Diagnostic and Statistical Manual of Mental Disorders; GABA: Gamma-Aminobutyric Acid; GSH: Glutathione; NO: Nitric Oxide; NOS: Nitric Oxide Synthase; SOD: Superoxide Dismutase; SPV: Superfluid Physical Vacuum; SSADHD: Succinic Semialdehyde Dehydrogenase Deficiency; SSRI: Selective Serotonin Reuptake Inhibitors; WHO: World Health Organization

Introduction

Autism (from the Greek *αὐτός* meaning 'self') was first described in 1911 by the Swiss psychiatrist Paul Eugen Bleuler. Bleuler postulated that this condition is characterized by a loss

of contact with reality and the existence of mutually exclusive contradictions within the psyche [1], and belongs to the group of schizophrenias. Over the years, the idea of autism has undergone numerous transformations, some of which diametrically oppose to each other [2]. The efforts to define and differentiate the various forms of autism failed, that's why the World Health Organization (WHO) introduced the general term of 'autism spectrum disorders' (ASD) – a range of conditions characterized by some degree of impaired social behavior, communication and language, and a narrow range of interests and activities that are both unique to the individual and carried out repetitively.

Epidemiology

The exact prevalence of ASD varies from study to study and from country to country. According to WHO, 1 in 160 children on a world scale, has an autism spectrum disorder [3]. ASD occur in all races, continents, social and economic groups and are about 4 times more common among boys than among girls [4].

Aetiology and Pathogenesis

The exact causes and mechanisms of occurrence of neurodevelopmental autistic disorders remain unknown. It is believed that ASD occur as a result of a complex interplay of genetic (copy number variations, such as deletions, duplications, inversions, or translocations), and environmental factors [5]. Among the potential genetic disorders are fragile X syndrome, tuberous sclerosis, Rett syndrome, etc. The environmental factors are classified as pre-natal (congenital rubella syndrome, mother's teratogen exposure or exposure to pesticides), peri-natal (low birth weight, abnormal gestation length due to pre-term delivery, birth asphyxia with hypoxic-ischemic insult), and post-natal (autoimmune diseases, leaky gut syndrome, viral infections, amygdala development failure, oxidative stress, vitamin D deficiency, heavy metal toxicity, etc.).

The understanding of the ASD pathogenetic mechanisms is as complex as its aetiology. Several theories try to explain the occurrence of autistic disorders with early brain overgrowth and neural overconnectivity, reduced intracortical connectivity, defective neural migration to the cerebral cortex in the first 6 gestational months, unbalanced excitability-inhibitory networks, abnormal assembly of synapses and dendritic spines, immune disorders, altered calcium signaling, mirror neuron dysfunction, decreased levels of apoptosis, etc [6,7].

Clinical manifestations and diagnosis

ASD are diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) of the American Psychiatric Association (APA). Symptoms are complex and comprise experiencing difficulties in communication and interaction with other people, restricted interests and repetitive behaviors hindering the normal functioning in diverse areas of life. The diagnosis of ASD is usually made during the childhood (before 36 months of age) [8].

Contemporary Therapy

Children with ASD require a comprehensive multimodal approach. The treatment should start as soon as the diagnosis is established. The main purpose of all therapeutic strategies is to reduce the disruptive effects of ASD on the individual functioning (learning, working, living and communicating with the others, etc.). A leading role in this aspect play the so-called 'behavioral', 'psychological', and 'educational' therapies with the active participation of psychiatrists, psychologists, speech-therapists, biologists, etc [8].

Pharmacological treatment plays a secondary role in the management of ASD. It can affect some of the symptoms (irritability, aggressiveness, hyperactivity, etc.) and the comorbid conditions but provides no causal therapy. Among the drugs used in patients with ASD are some antipsychotics (risperidone,

aripiprazole, clozapine), D2 receptor antagonists (haloperidol), selective serotonin reuptake inhibitors (SSRI) (sertraline), etc [9,10].

Materials and Methods

Novel Hybrid Approach

We introduce a novel approach for the treatment of children with ASD, combining the favorable effects of the 'cavity structure effect' and the oral intake of *Syringa vulgaris*-derived preparations. This regime could be independently used or as an addition to the already established treatment regimes.

Cavity Structure Effect

The Cavity Structure Effect (CSE) (also referred as Cavernous Structure Effect) was observed and described by two scientists – Oskar Korschelt and Victor Grebennikov.

Oskar Korschelt was a German industrial chemist who taught at the Medical University of Tokyo. In 1893 he obtained from the German Imperial Patent Office a patent for an apparatus utilizing cavity structures for treatment purposes (Patent No. 69340, granted on June 22, 1893). Korschelt constructed his device out of copper chains and plates, and treated with it patients with gastrointestinal problems, nerve disorders, insomnia and pain. He believed that his apparatus 'collects' certain type of rays from the environment and directs them to the patient [11].

Approximately a century later, the Russian entomologist Victor Grebennikov observed the CSE in nature during one of his expeditions. He studied the structure of diverse beetle wings, honeycombs, stalks of wheat, flowers etc., and actually gave the name of the CSE phenomenon. Grebennikov, just like his 'predecessor' Korschelt, constructed a device intended for medical purposes, whereas his device consisted of empty bee combs.

Both scientists documented a favorable effect in patients, subjected to the influence of their apparatuses but couldn't explain the mechanism of action of their machines. However, Korschelt and Grebennikov believed that, intentionally or unintentionally, people had always used or had always been exposed to the CSE (building and living in polygonal premises, such as the Asian pagodas, or wearing rings, diadems, bracelets, composite ornaments, etc.) [12].

Use of biologically active substances

The second part of the approach we suggest, includes the oral intake of biologically active substances (BAS) of natural origin. We describe the role of preparations derived from *Syringa vulgaris* (common lilac) in the treatment of children with ASD.

Botanical description. The common lilac belongs to the *Syringa* genus and the Oleaceae (Olive) family. It grows in temperate world areas and is native to Eastern Europe and Asia.

However, lilacs are grown all over the globe as garden hedges. The common lilac is a perennial, deciduous shrub which reaches 6 m of height [13] and blooms in May. Seeds ripen in August. The species is hermaphrodite and is pollinated by bees and Lepidoptera [14]. The leaves are simple, ovate to broadly ovate, and 5-12 cm long. The flowers are mostly white, lilac, or purple, pleasantly fragrant in long terminal panicles. The fruiting capsules are 1-1.5 cm long, with flat winged seeds. Common lilac prefers neutral to slightly acid soils and warm, sunny locations [15].

Our case series

In an attempt to prove the favorable effects of the exposure to the CSE and the oral intake of BAS of natural origin, we performed the following experiment: with the approval of their parents, we treated 4 children with ASD (0-5 years of age) for a period of 5 years with a novel approach, combining the findings of Korschelt and Grebenikov under conditions similar to the ones described by both scientists, and an oral intake of *Syringa vulgaris*-derived preparations.

In order to expose the children to the CSE, we fixed on the attic of patients' home (in the room where the children spend most of their time), three layers of hexagonal prisms (resembling honeycomb) and observed a progress in their communicational abilities and general individual functioning (behaviour, learning abilities, etc.). A computed schematic model of one layer of the hexagonal structures we used is represented in Figure 1.



Figure 1: A computed schematic model of one layer of the hexagonal structures used in the experiment.

Treatment regime

As far as we know, to this date, no reliable pharmaceutical product based on *Syringa vulgaris*, has been released on the market. That's why we offer the following way of preparation and application in accordance with child's age.

In children up to 12 months of age: 1-2 g of air-dried *Syringa vulgaris* blossoms are poured with 100 ml of boiled water. The mixture is allowed to stay for 30 minutes and should then be filtered. This amount is enough for 10 days for children up to 2 months of age, 5 days for children up to 6 months of age, and 3 days for children up to 12 months of age. For the daily doses, see (Table 1).

Child Age	Dosis
Up to 2 Months	10 ml once daily
Up to 6 Months	20 ml once daily
Up to 12 Months	30 ml once daily

Table 1: Daily doses of *Syringa vulgaris* water solution for children up to 12 months of age.

In children from 1-7 years of age, we recommend the use of a *Syringa vulgaris* alcohol extraction which is prepared as follows: 100 g of fresh *Syringa vulgaris* blossoms are poured with 1000 ml of 40% alcohol. This solution represents a 10% *Syringa vulgaris* tincture. For the daily doses, see (Table 2).

Child Age	Dosis
1-2 Years	1-4 drops three times daily mixed with water
2-3 Years	4-8 drops three times daily mixed with water
3-7 Years	8-12 drops three times daily mixed with water

Table 2: Daily doses of *Syringa vulgaris* tincture for children 1-7 years of age.

Results

In a series of 4 cases (children with ASD at the age of 0-5 years) our method showed over a period of 5 years (treatment period) an improvement in the overall performance after exposure to the CSE and oral administration of *Syringa vulgaris*-derived preparations (learning ability, communication skills, etc.), assessed by their leading therapist (psychologist, psychiatrist, etc.) using the Autism Treatment Evaluation Checklist (ATEC). Patient characteristics (at baseline, Year 0) are described in (Table 3).

No.	Sex	Age
1	Male	2
2	Female	3
3	Female	3
4	Male	5

Table 3: Patient characteristics at Year 0.

The Autism Treatment Evaluation Checklist (ATEC) is an internationally utilized and validated assessment tool, created to provide a quantitative evaluation of the ASD treatment process. It is a caregiver-administered questionnaire designed to measure changes in the ASD severity in response to the treatment applied which should be completed by parents, teachers, therapists, etc. ATEC contains 4 subscales – Speech/Language/Communication (14 items, 0-28 points), Sociability (20 items, 0-40 points), Sensory/

Cognitive awareness (18 items, 0-36 points), and Health/Physical Behavior (25 items, 0-75 points). Each patient is assessed and designated certain score for each subscale as the final total score represents a sum of all subscale scores (maximum 179 points). A lower score indicates a lower ASD severity.

We measured the ATEC scores of our patients at Year 0 (at baseline), 2.5 years after the start of the treatment and at the end of the treatment period (Year 5), and observed a stable decrease, as seen in Table 4. No side effects were observed.

Subject No.	ATEC Score		
	Year 0	Year 2.5	Year 5
1	90	64	40
2	86	55	40
3	103	68	45
4	110	85	42

Table 4: Autism Scores at baseline (Year 0), in the middle (Year 2.5) and at the end of the treatment period (Year 5).

N.B. We believe, that this treatment regime is suitable only for children up to 7 years of age, because of the theoretical possibility to influence the nerve system development at this stage of the individual development. Furthermore, the treatment should start as soon as possible after diagnosis establishment and should be carried out under strict medical surveillance.

Discussion

Physical basis of the Cavity Structure Effect

The possible explanations of the CSE, given by Korschelt (mobilization of vital forces) and Grebennikov (de Broglie waves) may seem insufficient to the contemporary reader. To the extent of our knowledge, there is only one article which scientifically hypothesizes the physical mechanism of action and the way CSE influences biological structures [12].

According to Boldyрева, the positive effect of the cavity structures could be explained by the presence of physical vacuum inside them, possessing the properties of the ³He-B (B-Phase Helium-3) superfluid. This type of physical vacuum is called superfluid physical vacuum (SPV). Supposedly, cavity structures (CS) are filled with spin supercurrents whose energy could be transferred to biological objects, when positioned inside them.

It has experimentally been proven that the different orientation of the CS with respect to human body, or biological objects at all, produces different effects. In CS, spin supercurrents of biological objects and CS interact in a physical vacuum (not in a molecular medium). These spin supercurrents may not be

shielded by molecular substances (screens). Also, after removing the CS from its position an after-effect is observed. This could be explained with the fact, that CS in the SPV form a ring of spin structures (quantum vortex ring) which in the stationary state in the superfluid does not diffuse, and respectively, doesn't disappear after removing the CS. The magnitude of the spin supercurrents depends on the characteristics of spin structures between which spin supercurrents arise, i.e. it depends on the material of which CS are made.

In our experiment, we decided to use hexagonal prisms (prisms with two hexagonal bases and six rectangular sides) as cavity structures. Hexagonal prisms are widely distributed in nature (honeycombs, chemical compounds, atomic structures, viral envelopes, etc.) which makes them a 'preferred' form of organization.

The most popular hexagonal shape are honeycomb cells. Mankind has been asking itself for centuries why bees prefer to build their homes and honey storage compartments as hexagonal prisms. Although the answer remains still unknown, mathematics succeeded, to a certain extent, to provide a reasonable explanation. Only three equal-side and equal-angle shapes could be used for a regular tessellation (tiling of a plane or surface) – equilateral triangles, squares and regular hexagons. Among them, hexagons provide the most efficient way of tessellation with the least effort and resource consumption. This fact turns bees into nature's most perfect mathematicians. That's why, Charles Darwin called honeycombs 'masterpieces of engineering' in his book 'On the Origin of Species'. Honeycomb lattices are used nowadays as filters in electronics, lasers, etc. Grebennikov used hexagonal prisms in his experiments, too.

The possible effect of honeycomb lattices could also be explained by their so-called 'natural' or 'eigenfrequency' – the frequency at which a system tends to oscillate in the absence of any driving or damping force. Experiments showed that honeycomb structures exert natural frequencies of ca. 5.8, 36.4 and 101.7 Hz, which partially coincide with the frequency of the brainwaves (neural oscillations) and probably stimulate them [16], especially theta and beta waves. Theta waves (4–8 Hz) move along the hypothalamus in a posterior–anterior direction and are related to memory (encoding new information) and spatial navigation [17]. Beta rhythm (13–38 Hz) is associated with the sensorimotor cortex, as well as with the cognitive functions [18].

Positive effects of chemical compounds of *Syringa vulgaris*

Contemporary phytochemical studies showed that the representatives of the *Syringa* species contain more than 140 secondary metabolites with an antitumor, antihypertensive, antioxidant and anti-inflammatory activity [19]. Among the BAS with a high concentration in *Syringa vulgaris* are glycosides (syringin), farnesol, iridoids, lignans, phenylethanoids, vitamin C, etc [20].

Syringin ($C_{17}H_{24}O_9$) is a natural plant metabolite (beta-D-glucoside, a monosaccharide derivative), isolated for the first time by Alphons Meillet in the 19th century. In animal experiments, syringin showed a regulatory activity on some biological indicators of oxidation, such as superoxide dismutase (SOD) and glutathione (GSH), thus removing harmful free radicals and preventing cell aging and cell death. In mice, syringin expressed certain anti-fatigue effect with an improvement of the spatial memory and learning ability [21]. The intragastric administration of syringin in animals decreased sleep latency and increased sleep duration (probably due to neutralization of the effects of the nitric oxide (NO) precursor L-Arginine and nitric oxide synthases (NOS)), which had a positive effect on the cognitive performance [22]. The inhibitory effect on the NO production could also explain the anti-neuroinflammatory properties of syringin [23,24].

Farnesol ($C_{15}H_{26}O$) is a 15-carbon, bioactive primary acyclic sesquiterpene alcohol. It possesses certain neuronal voltage-gated Ca^{2+} channel blocker properties and is active in alcohol withdrawal seizures. Farnesol is an antiepileptic agent, a positive allosteric modulator of gamma-aminobutyric acid (GABA) A receptors and suppresses seizures under experimental conditions in inherited succinic semialdehyde dehydrogenase deficiency (SSADHD) [25]. At hyperpolarized membrane potentials, farnesol induces a relatively non-selectable peak current inhibition of transiently expressed high voltage-activated Ca^{2+} -channels. Also, it mediates a selective, high affinity inhibition of inactivated N-type channels, as elective effects on N-type channels occur at physiological farnesol concentrations. Farnesol could be the first endogenous high affinity ligand for voltage-dependent calcium channels at all [26].

Conclusion

Having in mind the growing need of effective treatment opportunities in modern neurology and being inspired by the observations of Korschelt and Grebennikov, we decided to imply their findings in a scientifically proven comprehensive approach, which could be applied additionally to the already known therapies without any harmful effects for the patients. Being convinced that phytotherapy (which has already gained certain level of acceptance in modern medicine and is subject to extensive international research) could be a good addendum to this, we added the oral intake of plant-derived metabolites to our strategy. The idea of combining both approaches is a result of long-standing research activities and experiments.

As a result, the treatment proposed in this paper proved to be beneficial for patients with ASD. Although the exact mode of action remains unknown, we believe that the positive effects originate from a nervous system stimulation and, to some extent, functional 'correction'. In order to confirm or reject the usefulness of this approach, we need blind, properly designed and randomized

studies with a greater number of patients.

We should acknowledge that our experiment was concentrated on the clinical effects of the proposed regime and has some limitations, such as the small number of the participants, the lack of biochemical examinations (routine blood tests, measurement of active metabolite levels in blood), etc. but we believe it is a good first step. As every beginning, we rely more on clinical observations and try to find a theoretical explanation of the results observed. We hope this paper provides a good basis for further scientific examinations and are willing to cooperate with scientists all over the world on large scale projects, concerning autistic disorders in childhood.

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Conflict of Interest

There are no financial conflicts of interest to disclose.

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