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POSSIBLE MECHANISMS OF TITANIUM SALT INFUSED PATCHES REMEDIATION OF AUTISM AND ATTENTION DEFICIT DISORDERS

MOGUĆI MEHANIZMI LEČENJA AUTIZMA I POREMEĆAJA NEDOSTATKA PAŽNJE UPOTREBOM NALEPNICA IMPREGNIRANIH TITANIJUMSKOM SOLJU

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Ključne reči

Autizam, poremećaj nedostatka pažnje, nalepnice impregnirane titanijumskom solju, model rezonantnog prepoznavanja.

Key words

Autism, Attention Deficit Disorders, Titanium Patches, Resonant Recognition Model.

Abstract

Autism is mental disorder, diagnosable from early childhood, characterized by impaired communication and socialization, and repetitive behaviors, while Attention Deficit Disorder is characterised by inattention and attention deficit. Although the cause of these disorders is not well understood, there are some indications that it is associated with malfunction of development and functioning of neuro synapses due to mutations within proteins responsible for proper functioning of nerve cells synapses. In addition, there are some pilot clinical studies, that Autism and Attention Deficit Disorders can be remediated using Titanium Salt infused patches. Here, we applied the unique approach to explain how Titanium Salt infused patches can influence functioning of nerve cell synapses and consequently remediate Autism and Attention Deficit Disorders at molecular level using Resonant Recognition Model.

INTRODUCTION

Autism is mental disorder, diagnosable from early childhood, characterized by impaired communication and socialization, and repetitive behaviors. Along with the learning difficulties and limitations present in intellectually disabled, these characteristics may pose large burden on parents of disabled children. While there is no known cure for autism, certain behaviors may be managed by adherence to strict routines, regular consultations with health care professionals, and focus on alleviating the most detrimental symptoms[1-3].

The Autism Spectrum Disorder (ASD) is hereditary and is associated with malfunction of development and functioning of neuro synapses due to mutations within proteins responsible for proper functioning of nerve cells synapses[1-4]. On the other hand, Attention Deficit Hyperactivity Disorder (ADHD) is characterised by inattention (with and without hyperactivity) and attention deficit in young children but can extend throughout adulthood.

In recent studies, it has been shown that the titanium in pico-nanometer scale and soluble form has beneficial effects on health and reduction of pain [5,6]. One of such products is Tuning Element Behavioral Wellness Patches (Be-Well), that utilize electromagnetic frequencies. The frequencies in Be-Well patches are produced with Titanium Salt infused imprints and are passively transmitted through the skin contact. This type of imprinting technology is not new and is used often in electronics by imprinting microchips with different frequencies. Be-Well patches should be applied along

the spine close to neck or scull. Lasting from few days to about a week, they do not fall off, cannot be felt by wearer and can be worn in water. Be-Well is hypothesized to have potential benefits to children with behavioral disorders.

Based on this hypothesis pilot clinical studies have been done at Missouri State University (correspondence with prof. P. Durham), Green Pediatrics Integrative Clinic and Educational Center and Holistic Health Realities Clinic. Total number of children subjects (age 6-14) in these studies was 33 (22 boys and 11 girls). They were given Be-Well patch to wear for seven-day period, repeated for seven weeks. After 7 weeks the patch was not re-applied and final evaluations were performed after they had gone 7 days without patch.

So far, the standard method to measure behavioural disorders including autism and attention deficit is psychological evaluation using "behavioral scoring system". These children were evaluated weekly by their parents, using score system, on the following behavioural attributes: Focus/-Attention, Communication, Mood, Memory, Tantrums, Aggression, Appetite and Tics (if applicable). Overall scores were calculated through summation of scores for each aspect of the evaluation. This pilot clinical studies have shown steady increase in scores from week 1 to week 7, while week 8 showed slight drop in scores, which was reasonable to expect, as in this week subjects did not have Be-Well patch applied. These results are indicative that Titanium Salt infused Be-Well patches can improve condition of patients with behavioural disorders including autism and attention deficit.

Motivated by these results, we have investigated here the mechanisms of Be-Well patches remediation of Autism and Attention Deficit Disorders at molecular level. To achieve this goal, we have analysed synaptic proteins resonant frequencies using Resonant Recognition Model (RRM) and have investigated possibility of these frequencies to resonate with frequencies imprinted within Be-Well patches.

Methods and Materials

The whole variety of behavioural disorders can be generally classified in two groups: lack of interaction with outside world (Autism Spectrum Disorder – ASD) and inattention (with and without hyperactivity) (Attention Deficit Hyperactivity Disorder – ADHD). ASDs and possibly other behavioural disorders like ADHD are characterised by malfunctioning of proteins involved in nerve synapses. Thus, we concentrate on the activity of synaptic proteins and receptors associated with ASDs and their role in the pathogenesis of ASDs via synaptic pathways [4]. Synapses are defined as complex process of transferring information (signal) from one nerve to another. This process involves specific interactions of number of proteins both from pre- and post- synaptic nerve cells. There are two main different pathways in synapses: excitatory including developmental and inhibitory pathways [4]. Recent studies have found that synaptic related proteins such as Neuroligins (NLGNs) and Neurexins (NRXN) are associated with the development of ASDs [4]. Here, we primarily focus on the activity of synaptic proteins and receptors (Neuroligin and Neurexin), whose malfunction is crucial for development and pathogenesis of ASDs.

As interaction between Neuroligins and Neurexins is the most critical for synaptic functioning and as the most mutations relevant to ASDs are found in these two groups of proteins, we concentrated our analysis to these two groups of proteins and their interactions. In addition, ADHD is also neurodevelopmental disorder with unknown cause, but proposed to be related to autism and thus, we suppose that some sort of malfunction of neuro synapses could be also cause of ADHD. We have analysed both Neuroligins and Neurexins and their mutual interaction, using Resonant Recognition Model (RRM) to find out characteristic resonant frequencies of their activity and interaction and to propose that these frequencies can resonate with Titanium Salt infused imprints within Behavioral Wellness Patches (Be-Well).

Resonant Recognition Model

The RRM is based on the findings that certain periodicities within the distribution of energy of delocalized electrons along protein/DNA molecules are critical for protein/DNA biological functions and/or interactions with their targets [7,8]. If charge transfer through these macromolecules is introduced, then charge moving through macromolecular backbone can produce electromagnetic radiation, absorption and resonance with spectral characteristics corresponding to the energy distribution and charge velocity [7,8].

The RRM enables the calculation of these spectral characteristics, by assigning each amino acid a physical parameter representing the energy of delocalized electrons of each amino acid. Comparing Fourier spectra for this energy distributions by using cross-spectral function, it has been found that proteins sharing the same biological function/interaction share the same periodicity (frequency) within energy distribution along the macromolecule [7,8]. Furthermore, it has been shown that interacting proteins and their targets share the same characteristic frequency but have opposite phase at characteristic frequency [7,8]. Thus, it has been proposed that the RRM frequencies characterize, not only a general function, but also a recognition and interaction between the macromolecule and its target, which then can be considered as resonant recognition. This could be achieved with resonant energy transfer between the interacting macromolecules through oscillations of a physical field, which is electromagnetic in nature. Since there is evidence that proteins and DNA have certain conducting or semi-conducting properties, a charge moving through the macromolecular backbone and passing different energy stages, caused by different amino acid or nucleotide side groups, can produce sufficient conditions for a specific electromagnetic radiation or absorption. The frequency ranges of this field depend on the charge velocity. The RRM proposes that the charge is travelling through the macromolecular backbone at the estimated velocity of 7.87×10^5m/s [7,8]. For this velocity and with the distance between amino acids in a protein molecule of 3.8Å, the frequency of protein interactions was estimated to be in the range between 10^{13}Hz and 10^{15}Hz. Therefore, the estimated frequency range for both amino acid and nucleotide macromolecules includes infra-red, visible and ultra-violet light. To support this idea, we compared our computational predictions with number of published experimental results [7-12]. These comparisons have shown a

strong linear correlation between frequencies, as calculated using the RRM method and experimentally measured characteristic frequencies. This correlation can be represented as following:

$$\lambda = K / frrm$$

where λ is the wavelength of light irradiation in nm, which can influence particular biological process, frrm is a RRM numerical frequency and K=201 is coefficient of this linear correlation.

We applied this concept on number of proteins and DNA examples [9,10]. The concept has been also experimentally tested by predicting the electromagnetic frequencies for L-Lactate Dehydrogenase [12], where by radiating L-Lactate Dehydrogenase with predicted calculated electromagnetic frequencies the significant change in enzyme activity was achieved. The concept has also been tested independently on experimental measurements of photon emission from dying melanoma cells [13], on photon emission from lethal and non-lethal Ebola strains [14], as well as on classic signalling pathway, JAK-STAT, traditionally composed of nine sequential protein interactions [15]. Keeping all this in mind, we propose that the RRM concept is excellent predictor for proteins and DNA selective interactions, biological processes and pathways in living cells.

Frequencies calculated using the RRM, as described above, have been found to be related to biological function of the proteins. However, if we consider protein and DNA complex structures at different velocities [16,17]. Thus, with the same periodicities within proteins sequences, as determined by the RRM, different velocities of charge transfer can produce different resonant frequencies which not necessarily are related to the protein biological function but could be related to protein and DNA resonances in general.

Here, we have applied the RRM approach to proteins involved in nerve synapses with the aim to find out if there are possible resonances within these proteins that can resonate with Be-Well patches imprint frequencies and consequently can help in treatment of behavioural disorders.

Protein Sequences

The following protein sequences have been analysed using RRM from UniProt database:

Three Neuroligin1 proteins:

>sp|Q8N2Q7|NLGN1_HUMAN Neuroligin-1 OS=Homo sapiens GN=NLGN1 PE=1 SV=2
>sp|Q99K10|NLGN1_MOUSE Neuroligin-1 OS=Mus musculus GN=Nlgn1 PE=1 SV=2
>sp|Q62765|NLGN1_RAT Neuroligin-1 OS=Rattus norvegicus GN=Nlgn1 PE=1 SV=1

Three Neuroligin2 proteins:

>sp|Q8NFZ4|NLGN2_HUMAN Neuroligin-2 OS=Homo sapiens GN=NLGN2 PE=1 SV=1
>sp|Q69ZK9|NLGN2_MOUSE Neuroligin-2 OS=Mus musculus GN=Nlgn2 PE=1 SV=2
>sp|Q62888|NLGN2_RAT Neuroligin-2 OS=Rattus norvegicus GN=Nlgn2 PE=1 SV=1

Four Neuroligin3 proteins:

>sp|Q9NZ94|NLGN3_HUMAN Neuroligin-3 OS=Homo sapiens GN=NLGN3 PE=1 SV=2
>sp|Q8WMH2|NLGN3_MACMU Neuroligin-3 (Fragment) OS=Macacamulatta GN=NLGN3 PE=2 SV=1
>sp|Q8BYM5|NLGN3_MOUSE Neuroligin-3 OS=Mus musculus GN=Nlgn3 PE=1 SV=2
>sp|Q62889|NLGN3_RAT Neuroligin-3 OS=Rattus norvegicus GN=Nlgn3 PE=1 SV=1

Two Neuroligin4 proteins:

>sp|Q8N0W4|NLGNX_HUMAN Neuroligin-4, X-linked OS=Homo sapiens GN=NLGN4X PE=1 SV=1
>sp|Q8NFZ3|NLGNY_HUMAN Neuroligin-4, Y-linked OS=Homo sapiens GN=NLGN4Y PE=2 SV=1

Two α-Neurexin2 proteins:

>sp|Q9P2S2|NRX2A_HUMAN Neurexin-2 OS=Homo sapiens GN=NRXN2 PE=2 SV=1
>sp|Q63374|NRX2A_RAT Neurexin-2 OS=Rattus norvegicus GN=Nrxn2 PE=1 SV=3

Two β-Neurexin2 proteins:

>sp|P58401|NRX2B_HUMAN Neurexin-2-beta OS=Homo sapiens GN=NRXN2 PE=1 SV=1
>sp|Q63376|NRX2B_RAT Neurexin-2-beta OS=Rattus norvegicus GN=Nrxn2 PE=1 SV=1

Three α-Neurexin3 proteins:

>sp|Q9Y4C0|NRX3A_HUMAN Neurexin-3 OS=Homo sapiens GN=NRXN3 PE=1 SV=4
>sp|Q6P9K9|NRX3A_MOUSE Neurexin-3 OS=Mus musculus GN=Nrxn3 PE=1 SV=2
>sp|Q07310|NRX3A_RAT Neurexin-3 OS=Rattus norvegicus GN=Nrxn3 PE=1 SV=1

RESULTS

As pilot clinical studies, mentioned in Introduction, indicate that Be-Well patches have beneficial effect on autism and other behavioural disorders, we have investigated here the possible mechanisms of this beneficial effect at the molecular level.

As it has been proposed, that the main cause of ASDs and possibly ADHD is malfunctioning of neural synapses and interaction between Neuroligins and Neurexins, we have concentrated on analyses of Neuroligins, Neurexins and their interactions using RRM model, with the aim to find out the characteristic frequencies of such interactions. Once when such characteristic frequencies have been found, it can be proposed that Titanium Salt infused imprints within Be-Well patches can resonate with these frequencies, improve neural synapses normal functioning and consequently alleviate symptoms of ASDs and control ADHD.

Having in mind that ASDs appears in early childhood and thus could be considered as developmental disorder, we have initially analysed activity of Neuroligin3, which was found to be critical in development of synapses [1,2,4]. When the RRM model is applied to mammalian Neuroligin3 proteins the common characteristic frequency appears at fe=0.4155, as presented in Figure 1.

To make sure that this frequency is characterising, not only Neuroligin3 proteins, but also interaction between Neuroligin3 and corresponding Neurexin's, which is critical for proper functioning of synapses, we have compared Neuroligin3 proteins with corresponding Neurexin proteins.

The frequency of fe=0.4155 became more prominent, as presented in Figure 2. According to RRM principles, this

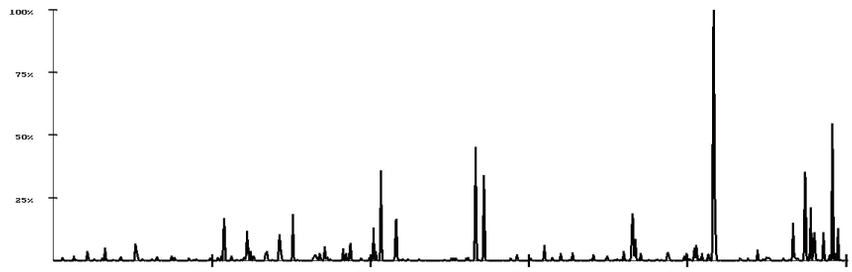

Figure 1. RRM cross-spectrum of Neuroligin3 proteins.

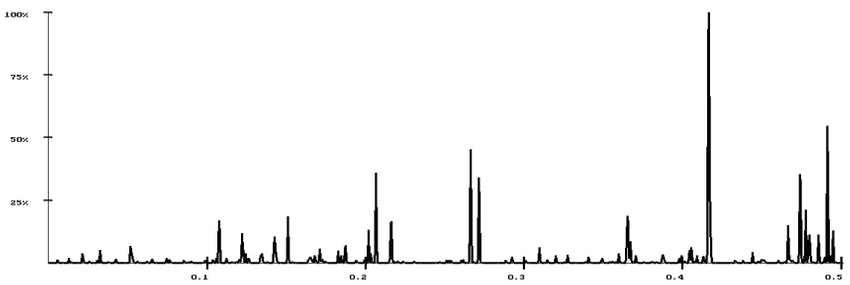

Figure 2. RRM cross-spectrum of Neuroligin3 proteins and α-Neurexin3 proteins.

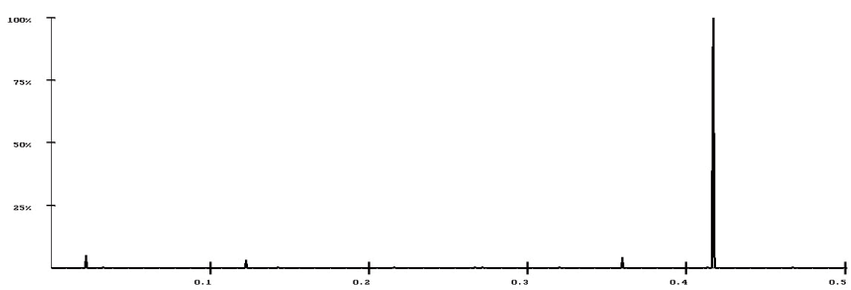

Figure 3. RRM cross-spectrum of Neuroligin proteins, including Neuroligins1, 3 and 4.

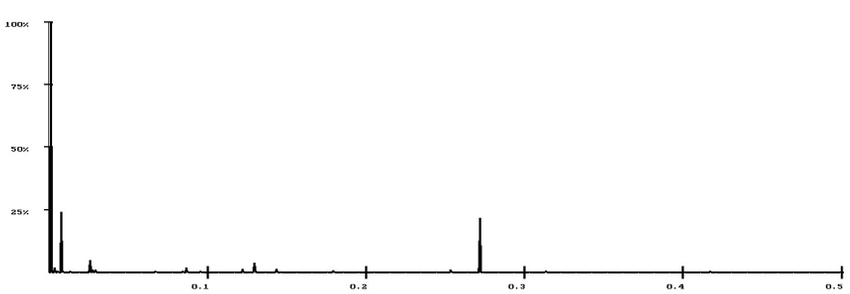

Figure 4. RRM cross-spectrum of Neuroligin2 proteins and α- and β- Neuroxin2 proteins.

frequency is characterising interaction between Neuroligin3 proteins and corresponding α-Neurexin3 proteins.

The next step was to find out what would be the characteristic RRM frequency for not only development of synapses, but also for their normal functioning. For that purpose, we have initially compared Neuroligin1, 3 and 4 proteins, which are all involved in excitatory synapse maturation and function. Interestingly the same RRM characteristic frequency of fe=0.4155 appeared common to all analysed Neuroligin proteins, as presented in Figure 3. These results are pointing out that the same RRM characteristic frequency is characterising both development and normal functioning of excitatory synapse.

Once when this characteristic RRM frequency was identified, we can calculate relevant wavelength of related electromagnetic radiation using the formula: λ = K / frrm. The wavelength related to the frequency relevant for development and functioning of nerve synapses is then λe=484nm. Thus, Titanium Salt or any other conductive particles in the Be-Well patches, that are in diameter of about Dλe=484nm, Dλe/2=242nm and Dλe/4=121nm, can resonate with synaptic proteins, influence development and normal functioning of nerve synapses and consequently remediate development and symptoms of ASDs.

On the other hand, inhibitory synapses formation and function goes through completely different pathway than excitatory synapse function and it involves Neuroligin2 and its corresponding Neurexins. When Neuroligin2 proteins were compared with corresponding Neurexin proteins completely different common characteristic RRM frequency appeared at fi=0.0015, as presented in Figure 4. This is very interesting result showing that excitatory and inhibitory synapses pathways have completely different RRM characteristic frequencies.

Once when this characteristic RRM frequency was identified, we can calculate relevant wavelength of related electromagnetic radiation using the formula: λ = K / frrm. The wavelength related to the frequency relevant for inhibition of nerve synapses is then λi=64000nm. Thus, Titanium Salt or any other conductive imprints in the Be-Well patches, that are in length of about Dλi=64000nm, Dλi/2=32000nm and Dλi/4=16000nm, can resonate with inhibitory pathway of synaptic functioning.

It is well known that ASDs are neurodevelopmental disorder, which is the most probably related to the functioning of developmental and excitatory synaptic pathway. Hence, we propose that characteristic RRM frequency of fe=0.4155 for developmental and excitatory synaptic pathway is the most relevant to be targeted for any proposed remediation of ASDs.

Having in mind that ASDs is characterised by lack of communication and restricted interest, while ADHD is characterised by inattention (with or without hyperactivity), we propose that ASDs is related to malfunctioning of developmental and excitatory synaptic pathway, while on the contrary ADHD is related to malfunctioning of inhibitory synaptic pathway. Thus, RRM frequency of fi=0.0015 for inhibitory synaptic pathway is the most relevant to be targeted for any proposed remediation of ADHD.

To find out, if there are other resonant electromagnetic frequencies that can influence development and excitatory

functioning of synapses, we have introduced other velocities of charge transfer through proteins, as described in Methods. When different velocities of charge transfer were applied to RRM characteristic frequencies of fe=0.4155, identified to be related to development and excitatory functioning of nerve synapse and fi=0.0015, identified to be related to inhibitory functioning of nerve synapse, the following resonant frequencies have been identified for each velocity, as presented in Table 1.

RRM Frequency	velocity as per RRM $7.87x10^5$ m/s	velocity as per Yomosa 3.2m/s	velocity as per Yomosa $1.2x10^5$m/s	velocity as per Pang 68m/s	velocity as per Davydov 170m/s	velocity as per Ichinose 0.34m/s	velocity as per Ichinose $5x10^{-4}$m/s
Excitatory: 0.4155	426-436TH	1731-1772MH	65-66TH	37-38GH	92-94GH	184-188MH	270-277KH
Inhibitory: 0.0015	1.5-3.1TH	0.2-0.4MH	0.3-0.7TH	0.1-0.3GH	6-13GH	0.7-1.3MH	1-2KH

Table 1. Electromagnetic frequencies for different velocities of charge transfer through proteins.

These frequencies are proposed to be able to resonate and may influence with either developmental and excitatory or inhibitory pathway of nerve synapses. Thus, we propose that if these frequencies are imprinted in Be-Well patches then such patches can resonate with either developmental and excitatory or inhibitory pathway of nerve synapses. According to RRM principles all these results could explain the mechanisms how Be-Well patches remediate the ASDs disorders and could control ADHD.

CONCLUSION

Motivated by pilot clinical studies, which have shown that Titanium Salt infused Be-Well patches can improve condition of autism and attention deficit disorders, we have investigated the possible mechanisms on how Be-Well patches achieve behavioural improvements in children using the RRM model. The approach was to analyse the synaptic proteins, whose malfunctioning could be cause of behavioural disorders, with the aim to find the characteristic resonant frequencies for development, excitation and inhibition of synapses and to investigate possibility of these frequencies to resonate with frequencies imprinted within Be-Well patches and consequently to propose mechanism of ASDs remediation and control of ADHD with Be-Well patches.

We found that:

Characteristic frequency for development and excitation of synaptic pathway is fe=0.4155. This numerical RRM frequency relates to electromagnetic wavelength λe=484nm. Thus, Titanium Salt or any other conductive particles in the Be-Well patches, that are in diameter of about Dλe=484nm, Dλe/2=242nm and Dλe/4=121nm, can resonate with synaptic proteins, influence development and normal functioning of nerve synapses and consequently remediate development and symptoms of ASDs.

Characteristic frequency for inhibition of synaptic pathway is fi=0.0015. This numerical RRM frequency relates to electromagnetic wavelength λi=64000nm. Thus, Titanium Salt or any other conductive imprints in the Be-Well patches, that are in length of about Dλi=64000nm, Dλi/2=32000nm and Dλi/4=16000nm, can resonate with inhibitory pathway of synaptic functioning. Having in mind that ASDs is characterised by lack of communication and restricted interest, while ADHD is characterised by inattention (with and without hyperactivity), we propose that ASDs is related to malfunctioning of developmental and excitatory synaptic pathway, while on the contrary ADHD is related to malfunctioning of inhibitory synaptic pathway. Thus, RRM frequency of fi=0.0015 for inhibitory synaptic pathway is the most relevant to be targeted for any proposed remediation of ADHD.

When different velocities of charge transfer through proteins is introduced, the resonant frequencies for development and excitation, as well as inhibition of synaptic pathway could then be in different frequency ranges including THz, GHz, MHz and KHz, as presented in Table 1. These frequencies could also resonate with frequency imprinted within Be-Well patches.

This work represents innovative approach to study mechanisms of Be-Well patches effects to ASD and ADHD at cellular and molecular level. The results of these study can support the idea that Be-Well patches could help patients through electromagnetic resonances between Titanium Salt infused patches and synaptic proteins to improve their behavioural disorder conditions without using drugs and their negative side effects.

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Sažetak

Autizam je mentalna bolest koja se dijagnostikuje u ranom detinjstvu i ispoljava se sa problemima u komunikaciji i socijalizaciji, i ponavljajućim ponašanjem, dok je poremećaj nedostatka pažnje karakterisan nesposobnošću pacijenta da se fokusira sa ili bez hiperaktivnosti. Iako uzrok tih poremećaja nije sasvim poznat, postoje neke indikacije da je povezan sa poremećajem u razvoju i funkcionisanju nervnih sinapsi uzrokovanom mutacijama u proteinima koji su odgovorni za pravilno funkcionisanje sinapsi medju nervnim ćelijama. Istovremeno neke preliminarne kliničke studije su pokazale da nalepnice impregnirane titanijumskom solju mogu pozitivno da utiču u lečenju autizma i poremećaja nedostatka pažnje. Koristeći model rezonantnog prepoznavanja, mi smo u ovom radu primenili jedinstveni pristup u objašnjenju kako nalepnice impregnirane titanijumskom solju utiču na rad nervnih sinapsi i tako potpomažu u lečenju autizma i poremećaja nedostatka pažnje na molekularnom nivou.

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