Intranasal Proinsulin C-peptide:

PARADIGM SHIFT IN HEALTH PROTECTION AND HEALING?

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Abstract

The first beauty-care product containing proinsulin c-peptide was launched two years ago and it is available in the market since that time. A number of people tried using it off-label, as a nasal spray, similarly to the intranasal insulin. The experiences gathered during the past two years are astonishing and surprising.

The present study is already the second retrospective case study, in which the wide range of experiences are introduced. Complementing the first case-study now it is demonstrated through the experiences of 90 users that the effect of proinsulin c-peptide refers to a wide range of recovery in the central nervous system. This is the only explanation that this drug can be beneficial not only in developmental disabilities, autisms, etc. but also in cases of hypertension, stroke and traumatic brain injury. The importance of this is invaluable, since such a tool for regenerate the impairments of the central nervous system hasn't been available until now. This is why it was not fully known in what cases and to what extent can the regeneration of the nervous system be effective. This unique opportunity may be important in the present COVID 19 pandemic, since the regeneration of the nervous system is crucial in this problem area as well, in defeating both the disease and the short- and long-term complications.

Introduction

The potential role of proinsulin c peptide in brain development: possibilities for intervention

Proinsulin c peptide is produced in placental tissue even in mothers with diabetes type 1 (T1D). This may mask the lack of c peptide production for the fetus in the body of the mothers. [i] Although the brain is also producing insulin and c peptide independently of the pancreas, the lack of c-peptide secreted by pancreatic cells may have developmental consequences for the children born to mothers with insulin dependent diabetes mellitus. [ii]

The risk of autism spectrum disorder (ASD) in offspring born to mothers with T1D is significantly elevated even compared to mothers with diabetes type 2 (T2D) and mothers with gestational diabetes (GDM). "Relative to no diabetes exposure, the adjusted HRs for exposure to maternal diabetes were 2.36 (95% CI, 1.36-4.12) for T1D, 1.45 (95% CI, 1.24-1.70) for T2D, 1.30 (95% CI, 1.12-1.51) for GDM by 26 weeks' gestation, and 0.99 (95% CI, 0.88-1.12) for GDM after 26 weeks." [iii]

Remarkably, autonomic dysfunction and reduced heart rate variability (HRV) is observed in individuals with ASD and with T1D as well. [iv] [v] [vi]

The supplementation of proinsulin c peptide for patients with T1D improves autonomic function and increases HRV. [vii] This effect may be also achieved even more efficiently by the central/intranasal administration of c-peptide. [viii] [ix] It may be also relevant that higher HRV is related to better expressive and receptive language in ASD children [x]

Proinsulin c peptide may inactivate cofilin, the actin separating protein that is important for early brain development. [xi] The lack of proinsulin c-peptide may predispose cofilin to be excessively activated and that may cause early growth cessation of the hippocampus. [xii]

Indeed, one of the most promising methods of improving the symptoms of ASD suggested by investigators is the inactivation of cofilin in neurons. [xiii]

Neuroinflamation is associated with ASD. [xiv]

In this respect it is of relevance that cofilin deactivation reduces the inflammatory processes associated with microglia, the brain resident immune cells. [xv]

The above outlined mode of action of C-peptide that is implemented in the central nervous system indicates that it likely activates the cholinergic anti-inflammatory pathway and provide beneficial influence on a wide range of inflammatory diseases. Our study highlights the hypothesis that the symptoms of several diseases can be eased through influencing the activity and the immune state of the nervous system.

Applied proinsulin C peptide spray

The participants of our study were using the Vargapeptide skin-spray off label, as an intranasal spray, on their own responsibility. The spray is produced and distributed by the Max-Immun Ltd.
This was applied in the same way as the intranasal insulin was and is administered in the population of children with Phelan-McDermid syndrome. A 20 ml bottle contains a solution of 18 ml C-peptide.
One puff off the spray contains 0,108 mg proinsulin C-peptid. In Vargapeptide 0,5 this amount is half, 0,05 g, in Vargapeptide 2 the amount is 0,216 mg.
The spray contains 0,8 % NaCl. The other ingredients fulfill the requirements of pharmaceutical grade purity. The purity of proinsulin C-peptid is 98-99%.

The range of dosages in the cases of autisms, ADHD and behavioral disorder was from 1 X marked Vargapeptide 1 - 0,5 blow to 3 - 4 X blow of Vargapeptide 4. The duration of treatment was from 1,5 to 13 months.
The range of dosages in the cases of the following diseases: neurological, autoimmune tumor, MRSA, psoriasis, migraine, FOG, arthritis, psychiatric diseases was from 1 X Vargapeptide 0,5 to 8 X Vargapeptide 2 daily. The duration of treatment was from 1 to 18 months.

Autisms spectrum disorder (ASD)

Autisms spectrum disorder (ASD)

- Sleep-wake cycle, sleep quality, level of arousal
- Eating, fluid intake, appetite, quantity and quality of digestion
- Movement (fine motor, gross motor functions)
- Cognitive abilities (attention, interest, memory)
- Learning (reading, writing, keeping rules, discipline)
- Speech and communication (speech comprehension, expressive speech, nonverbal communication)
- Emotional state: mood, ability to being calmed down, expression of feeling
- Social skills (contacts with acquaintances, showing interest in other people)
- Behavioral disorders, neurological symptoms (stereotype behavior)
- Independent living skills (eating, dressing, toilet use)

Selection of cases concerning diseases

- Autisms spectrum disorder
- ADHD
- Developmental delay
- Behavioral disorder

The list of selected cases according to the disease groups is presented in Table 1.

Evaluation

The effect of C-peptide treatment was significant improvement in all areas that were selected for investigation. On one hand these changes made it more bearable for the families of the selected persons to keep them in the family. The reduced sleeping disorders made everyday life easier. On the other hand the improved abilities in speech development created new opportunities in socialization and learning for the persons suffering from these diseases.

However it should be emphasized that this is a complex problem and it requires great professional knowledge and commitment for those who work in this field. The social and economic importance is at least as great as the human aspect of this problem affecting a rapidly increasing number of people.

Case	Age	Sex	Diagnose	Associated diseases
1.	3 years	male	Autistic disorder	Delayed speech development, Neurological immaturity
2.	3 years	male	Autisms spectrum disorder	
3.	4,5 years	male	Infantile autisms	Mixed specific developmental disorder, Leaky gut syndrome
4.	5 years	male	Infantile autisms	
5.	7 years	male	Autisms, speech apraxia	Anxiety, 17q12 deletion syndrome
6.	7 years	female	Autisms	Asthma
7.	7 years	female	Autisms	
8.	10 years	female	Autisms	
9.	10 years	male	Autisms	Mild learning disability
10.	10 years	male	Autisms	Mental retardation
11.	12 years	male	Autisms hyperacusis	Hyperacusis, Delayed motor and speech development
12.	12 years	male	Autisms	
13.	19 years	male	Autisms	Mild learning disability
14.	19 years	female	Autisms	
15.	26 years	male	Autisms	Epilepsy, Diabetes
16.	29 years	male	Autisms	Speech and behavioral disorder, Depression, Mental retardation
17.	38 years	male	Somatomental retardation	Meningoencephalitis, Renal stone
18.	6 years	male	ADHD, delayed speech development	Hyperacusis, Rhinitis allergica
19.	9 years	male	ADHD	Enuresis nocturna
20.	2,5 years	male	Developmental delay	
21.	9 years	male	Behavioral disability	Epilepsy, Auditory nerve lesion, Recurrent croup

Table 1. – Participants of the disease group of autisms spectrum disorder

Results

The demonstration of the results does not follow the list of the described aspects of investigation, but is discussed in the order of the importance of these fields concerning the life of the family and the part of the society. This is why sleeping comes in the first place and speech as the second one.

The information we gathered concerning these aspects were different in the different disease groups. One thing is that these disease patterns are different in severity and in their clinical features and also the associated symptoms lend new colors to the general picture, e.g. learning and sensory disabilities, diabetes, hypertension, etc. Also, there was a case where half of the small intestine was extracted.

Experiences gathered in the group of children with symptoms of autism spectrum disorder.

The parents of these children reported the following changes:

Sleeping

The reason why it comes first is because the adults in the family go to work and therefore the need to rest and sleep is crucial for them. Autisms, ADHD, and other behavioral disturbances are often accompanied by severe sleeping disorder. If they can't sleep, they can't fulfill their tasks appropriately and in the long run they may lose their job and be pushed out of the labor market. This means losing the second civil fundamental right, the right for work, since the right for rest is also a fundamental right. Furthermore chronic tiredness can serve as a basis for different health problems (psychic or physical diseases, and addictions as well.

Before the start of the C-peptide treatment 8 from the 21 slept well.
After applying the drug in 10 cases the inappropriate sleeping resolved. In 3 of these cases the shallow sleep became more calmer and more relaxed. In 7 cases the child, who previously had short time sleep, could not sleep over the night or woke up several times, after a few weeks their parents reported about restful night sleep Crying at night or waking up crying stopped in 1 case and also in 1 case bruxism decreased. In 1 case apnea ceased.

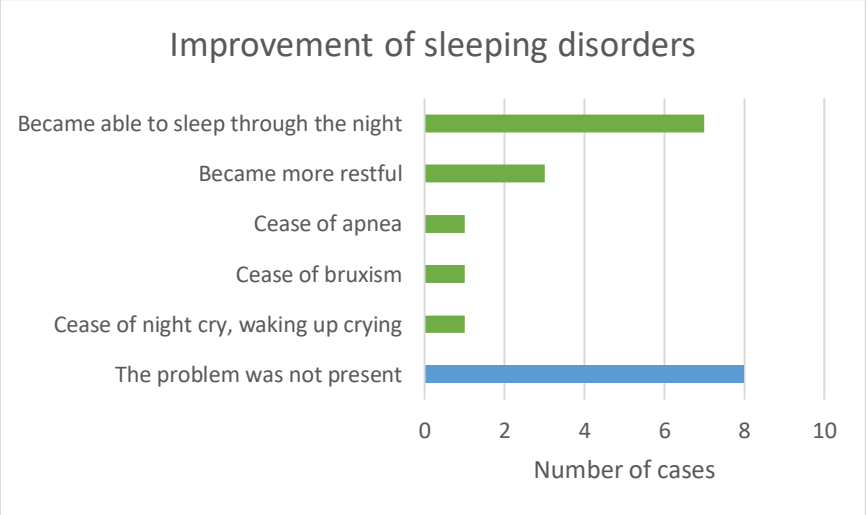

Figure 1. – Improvement of sleeping problems

Shallow sleep, waking-up at night or the short time sleep are extremely stressful for the child and for the family members as well. The resolved sleep may generate further positive changes in the aspects of investigation. The restful state of the child may have impact on better utilization of cognitive abilities, and due to this improvement in learning, or even a more calmer general behavior, as a few parents reported.

Speech and communication

Speech and communication is the basis, as well as a crucial condition of socialization, learning, change in cognitive abilities, independent skills and the development of motor skills. These factors influence the emotional state of the patient through the awakening and development of self-consciousness.

In our investigation, in the field of speech and communication we were interested in the changes in comprehension, expressive speech and also non-verbal communication.

With those children who could speak already, we counted the changes from their level of speech at the time when the family was questioned. In the case of each child we experienced increases in vocabulary, in children at the early phase of speech development the presence of new words, and in those who had only a few words, the constitution of simple sentences started. Out of the investigated 21 cases, two from the three verbal children could speak well earlier, in the third case the articulation disorder did not change. In the remaining 18 cases the improvement was moderate in 8 and significant in 10 cases, out of these children there was a remarkable improvement. This was usually accompanied by improvement in articulation.

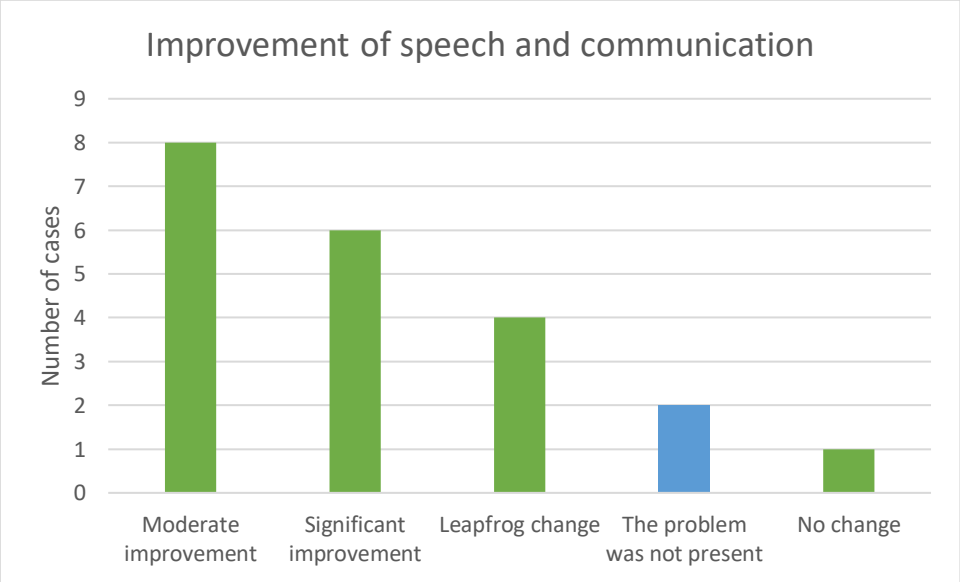

Figure 2. – Improvement of speech and communication

In those 8 cases showing moderate improvement four were non-verbal children. In two cases babble was changed by saying the first syllabus of the word. In two cases children started to imitate words. In the remaining four cases notable change did not happen concerning skills of cooperation compared to the level before applying the drug.

Out of the 10 cases who reported significant change, in one case „the child could say over 50 words instead of the earlier 2-3 words. He is a real chatterbox." Improvement in comprehension appeared active responses to speech in these cases. In one case for example after two weeks the child was temporarily speaking fluently for two days, than stopped.
According to the parents' reports the positive changes were observed a few days after the onset of applying the drug. Non-verbal communication was not investigated in each case. When it was questioned, the parents indicated the improvement or the start of eye contact. Others mentioned the improvement of eye gaze (conscious eye movements). These were evaluated as the improved attention.

In one child, who „could speak English fluently, formal speech error was improved: gabbling and stuttering decreased." In another child dysphonia improved, his speech became clearer."

In one case (29 year old person with autisms) comprehension improved so much, that „by now he asks questions and tells his observations".

Social skills

Developing eye-contact or keeping eye-contact for a longer time was reported by the parents as an important change. Those, who developed now, earlier did not make eye-contact, those who became able to keep eye-contact, looked into the eyes only for a short time, for one or two seconds. Keeping eye-contact - that means to look into the other's eye long and intensively – means that the child can observe the facial expressions, and thereby the ability of interpreting mimics starts, which is an important prerequisite of developing social skills.

Cooperation skills: In 10 cases the parents directly reported about the improvement of cooperation skills, there are 3 cases where the expressions „more opened for a hug" outbursts of anger decreased, „better mood" refer to the improvement of cooperation skills. In the cases of 11 persons there was no significant change concerning cooperative skills, compared to the state before applying the drug.

Integration to school: In two cases the parents reported about improvement, in 19 cases there was no significant change in terms of school integration, compared to the situation before applying the drug.

Rule keeping: this is in connection with the observed changes in the cooperation skills and in task management and behavior. In 12 cases the answers suggest improvement in keeping rules. In the remaining 9 cases there was no significant change concerning rule keeping compared to the situation before applying the drug.

Task awareness: 1In the case of 11 persons "task awareness improved". In 2 cases the child's behavior became more predictable, which can be considered as the improvement of task awareness. In the remaining 10 cases there was no significant change concerning task awareness compared to the situation before applying the drug

Mood, emotional awareness: There was a change in 8 cases, in 2 cases the outbursts of anger decreased, in 1 case ceased. Parents reported about a better mood in 3 cases, out of these in one case they were speaking about a new emotion appearing, the ability to show empathy.

In two cases the positive change covered not the relation with unknown people, but the attachment, bonding to family members: started to accept hugs, stopped to protest against being touched. In 13 cases there was no significant change concerning mood and emotional awareness compared to the situation before applying the drug.

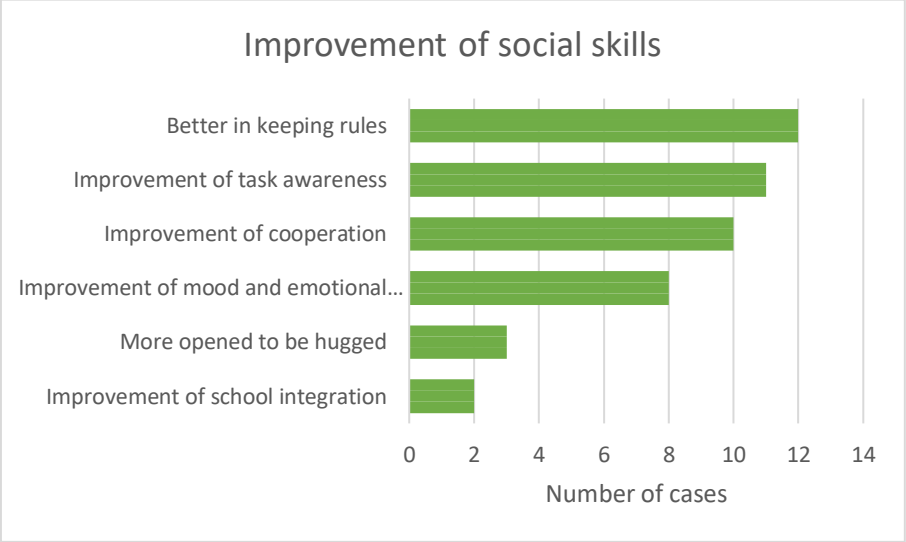

Figure 3. – Improvement of social skills

Overall some improvement was noticeable in each person without exception, in the majority of the cases they were significant, in a few cases moderate changes reported by the parents.

Cognitive abilities: attention, memory and learning

The two most important observations concerning cognitive abilities were the intensification of attention and in correlation with this, the improvement of memory.

Attention, orientation: In 13 cases improvement of attention was noticed. In 2 cases it was an indirect effect: the improvement of attention and orientation can be deduced from the improvement of learning skills and from „says when he wants something". In the remaining 8 cases there was no significant change concerning attention and orientation.

Memory: In 6 cases significant improvement of memory was indicated. The 7. parent reported that his 12 year old son „speaks 7 languages since the age of 3". These observations of the parents correlated with the teachers' judgments. In the cases of 14 persons no notable change occurred.

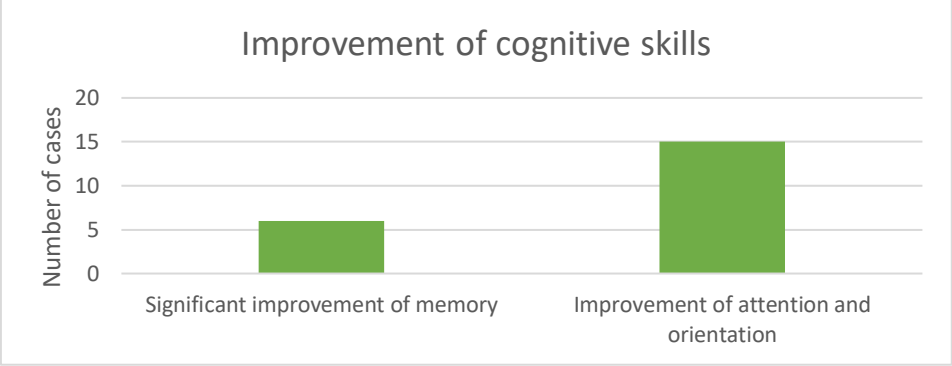

Figure 4. – Improvement of cognitive skills

Those children who had difficulties or were passive in reacting to verbal instructions, warnings, calling their names, started to give adequate feed-back, turned to the speaker and responded.
It is noticeable that certain skills that appeared as new achievement, can be the prerequisite of a more active appearance of other skills, e.g. auditory attention, positive response to a request, understanding and following an instruction.

Neurological symptoms: stereotypes, autistic behavior

Among the changes in the field of neurological symptoms the parents found the decrease in the number of outbursts of anger and in some cases the ceasing of them the most important, as it was described earlier under the heading „mood, emotional awareness", in the evaluation of social skills.
This was reported by 7 parents, for whom the outbursts of anger and mood fluctuation caused a lot of troubles.

Autistic symptom, ADHD: changes were noticed in 9 cases: 1) „The earlier maniac preference of pink color (straw, socks) is not characteristic any more". 2) „Reacts sensitively to front changes, hits his head with his hand or with an object", 3) „Autistic features decreased, became more opened". 4) „learned to clean his teeth". 5) „Stopped eating only a limited variety of foods". 6) „Expressed autistic symptoms since he had MMR vaccination at 15 months, no change in these 7) „Not vomiting from negative odor any more". 8) „Walking on tiptoe less frequently". 9) „Behavioral extremes" decreased.

Stereotypic behavior: 1) „Flapping hands became less frequent, 2) „Stopped the stereotypic spinning of toy car's wheels" wrote the parent, quoted earlier in point 8).

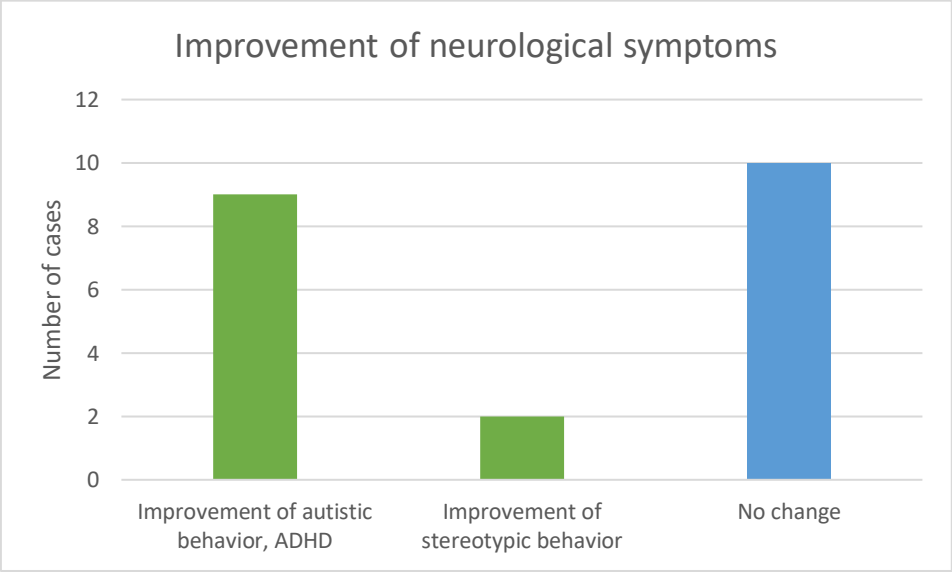

Figure 5. – Improvement of neurological symptoms

In summary 11 parents reported beneficial effects of the therapy concerning the investigated field: autistic symptoms, ADHD and stereotypic behavior. Among these in two cases the parents indicated that the stereotypic behavior (spinning wheels and flapping hands) ceased or became less frequent. In case of 10 people there was no notable change.

Emotional state

In the cases of 5 children they were nice and cheerful already before the treatment. 14 parents found important the decrease of mood swings and the improvement of mood in general in their children. Among these children one parent reported that it ended that her child woke up crying, and one parent said that „her child started to examine himself and his mother's face in the mirror". In two cases the parents did not notice any change.

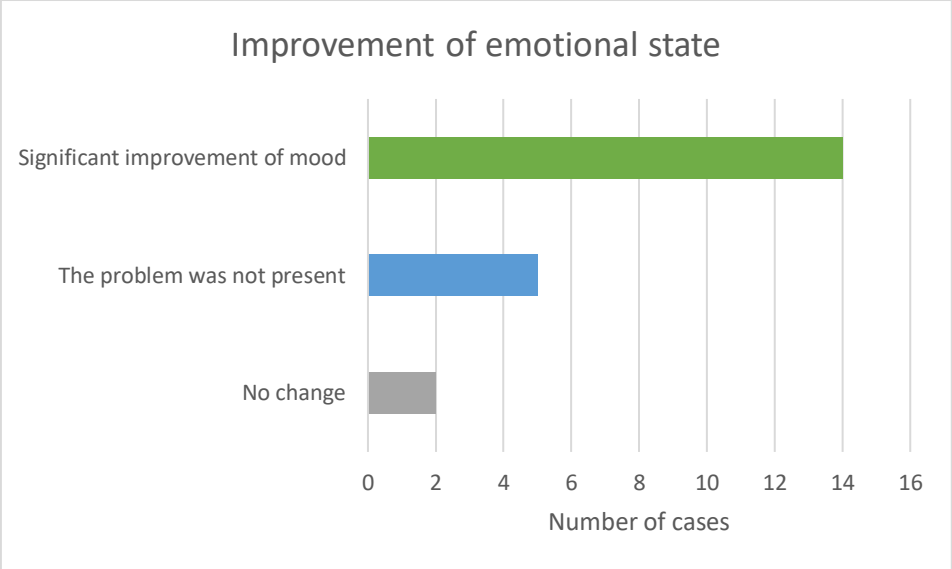

Figure 6. – Improvement of emotional state

Changes in learning abilities

Changes in learning abilities are obviously related with the improvement of attention skills, when it is already measurable. Therefore 4 parents could not answer this question. Also 4 parents indicated that their children already left school, don't attend school any longer.
7 parents gave positive answers to this question, the learning ability of their children clearly improved due to the C-peptide treatment.
In the remaining 6 cases there was no significant change concerning learning abilities compared to the situation before applying the drug.

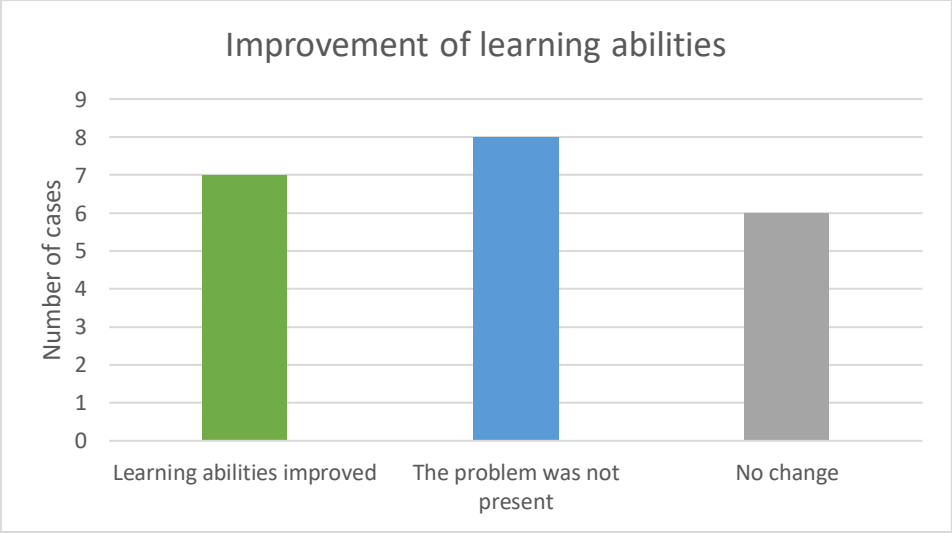

Figure 7. – Improvement in learning skills

Independent living skills

After treatment 9 participants reported improvement. The cases 2), 3), 4) and 5) said: „undresses independently 8) „takes off shoes when told to do so", 10) „putting on his trousers goes better", 11) „Great improvement in dressing", 13) „Improved in each skill, cleans his teeth already independently", 21) „Washing his hand already independently" (2,5 years old). 3 of the respondents said that their child was able to dress himself independently or with minor help before the treatment as well. The mother of one child responded that he is a wheel-chair user and still needs full care in everything. In 12 cases there was no significant change concerning independent living skills compared to the situation before applying the drug.

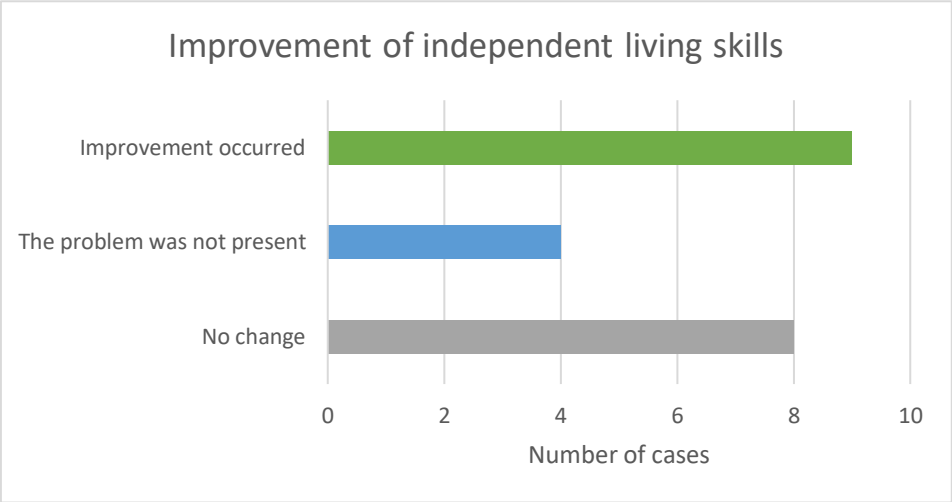

Figure 8. – Improvement of independent living skills

Motor skills

In the field of motor skills the parents reported in 17 cases that their children's walking became more stable and their balance improved. We'd like to highlight one case from the 17, where the parents said „earlier the child was running around while walking together, now he is coming next to us" and the parents also noticed increase in muscle tone. The mother of one child responded that he is a wheel-chair user and still needs full care in everything. In 4 cases there was no significant change concerning motor skills compared to the situation before applying the drug.

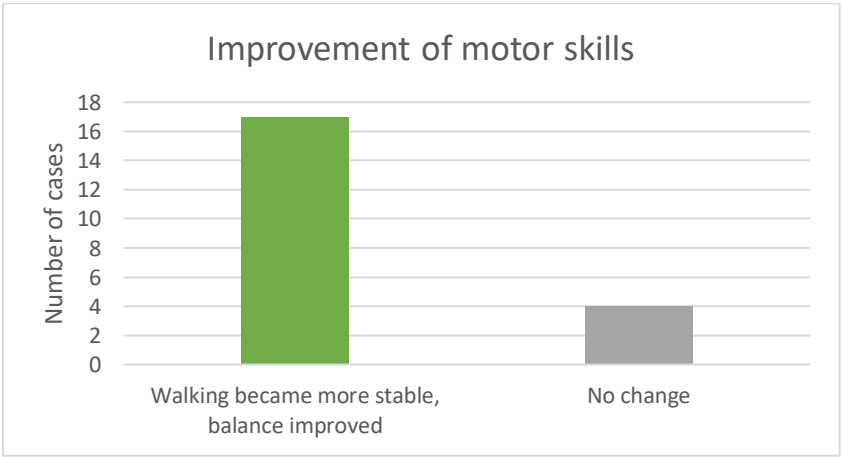

Figure 9. – Changes in motor skills

Appetite (eating-drinking), digestion, change in quantity and quality of defecation

There is no change in appetite; all of them have good appetite. According to selective eating it was mentioned in 4 cases that it decreased or ceased. In 2 cases selective eating remained.
In several cases constipation ceased, but there was also a case where the frequent, liquid defecation disappeared.

Experiences gained among children with symptoms of autisms spectrum disorder, consequences

Our investigation following the above mentioned aspects showed that significant change was noticed in each investigated aspect due to the C-peptide treatment.
These changes on one hand made it more livable for the family to keep the persons with this condition in the family. The reduced sleeping disorders made everyday life easier. On the other hand the improved abilities in speech development created new opportunities in socialization and learning for the persons suffering in these diseases.

Disease patterns in the field of internal medicine

Hypertension

There were eight participants in this group.

Case	Age	Sex	Diagnose	Associated diseases
1.	61 years	female	Hypertension	
2.	35 years	female	Hypertension	
3.	65 years	female	Hypertension	
4.	67 years	female	Hypertension	
5.	71 years	male	Hypertension	
6.	61,5 years	male	Hypertension	
7.	62 years	female	Hypertension	
8.	52 years	female	Hypertension	

Table 2 – Participants of the hypertension group

Evaluation concerning the investigated aspects

Fatigue: Out of 8 persons in 7 cases it has been reduced or ceased. 1 person did not have this symptom.

Neck, headache: In the case of 4 persons it ceased, 3 persons did not have this symptom, in 1 case it preserved.

Chest pain: In the case of 4 persons it ceased, 4 persons did not have this symptom.

Numbness of arm, face: In case of 2 persons it ceased, or improved. In case of 6 persons this symptom was not characteristic neither before the treatment.

Vision problem: In the case of 3 persons it ceased, or improved. In the case of 5 persons this symptom was not present

Tinnitus: In the case of 1 person it ceased, „appears rarely" In the case of 7 persons this symptom was not characteristic neither before the treatment.

Dizziness: In the case of 5 persons it ceased, or improved. In the case of 3 persons dizziness was not characteristic neither before the treatment.

Nose bleeding: It was not a characteristic symptom in the investigated group.

Elevated cholesterol: In the cases of 6 persons it has reduced, out of these in 1 case it reached normal range, in 1 case it was not measured again. In the case of 2 persons it was not higher before the treatment either.

Blurred vision: In the case of 4 persons it ceased, in the cases of 4 persons it was not present earlier either.

Change in the retina In the case of 1 person improvement was reported, the others did not have retinal problem.

Cervical vasoconstriction: In the case of 1 person it has improved, the others were not examined for this symptom.

Fast heartbeat: In the cases of 5 persons it has been reduced or ceased, in the cases of 3 persons fast heartbeat was not typical.

Swatting without reason: In the cases of 5 persons it has been reduced or ceased, in the cases of 3 persons fast heartbeat was not typical.

Pulsation in the temporal area: In the cases of 3 persons it has been reduced or ceased, in 5 cases there was no complain about it.

Concentration decline In the cases of 5 persons it has been reduced or ceased, in the cases of 3 people's concentration decline was not noticed.

Imbalance: In the cases of 3 persons it has been reduced or ceased, in 5 cases the patient had no imbalance problem.

Oedema: In the cases of 2 persons decrease, in 2 cases increase was reported, in 4 cases the patients had no oedema.

Load shortness of breath: In the cases of 7 persons it has been reduced or ceased, in 1 case this symptom was not typical.

Nocturia: Out of 4 persons it has ceased in 3 cases, in 1 case it has been reduced and in 4 cases it was not typical.

Stroke: stroke did not occur while applying the spray.

Heart attack: there was no heart attack while applying the spray.

RR average value: In the cases of 5 persons even the extremely high values returned to normal, 3 persons had normal tension.

Pulse: In the cases of 3 persons tachycardia ceased, in 5 cases the investigated persons had normal pulse.

Applied therapy: Those whose blood pressure was 280/120 Hgmm and 210/90 Hgmm, surprisingly they were able to stop taking all the three types of medicine. Also the patient who had a blood pressure of about 180/100 Hgmm, could also quit all the three types of blood pressure lowering pills. Those 4 patients, who were balanced with the help of only one type of blood pressure lowering pill, could also quit taking their pills. The patient, who had 150-170/80-90 Hgmm values without medication, his blood pressure values lowered to 100-110/60-70 Hgmm.

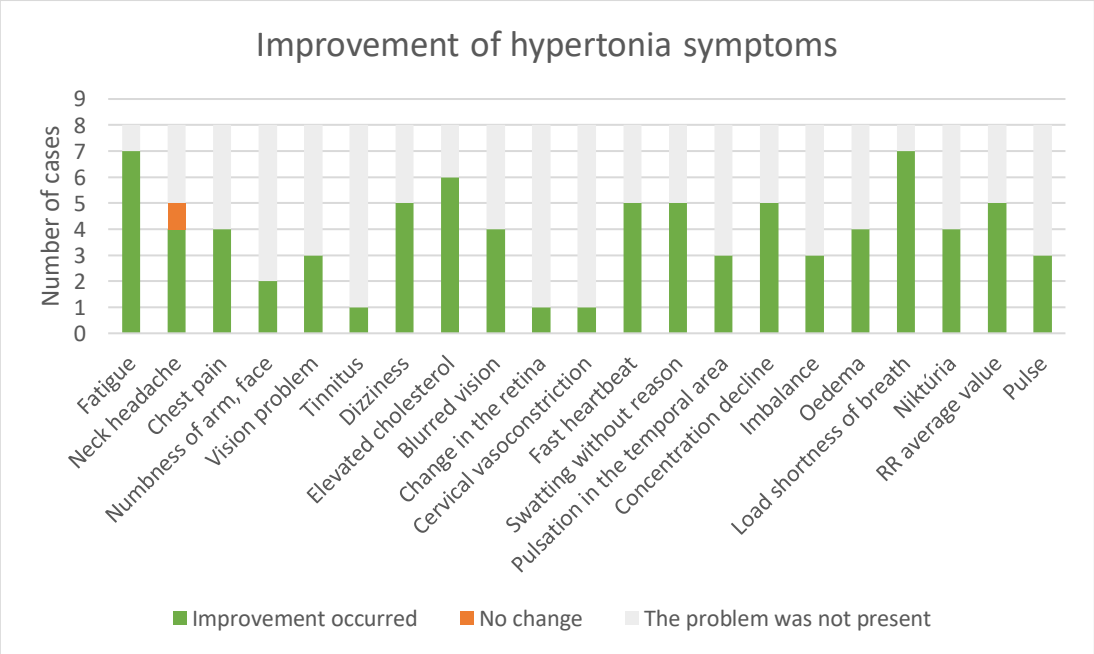

Figure 10. – Improvement of hypertension symptoms

Evaluation

In summary it is clear, that in all improvement appeared in the changes of blood pressure, compared to the discrepancies before the C-peptide treatment. All the improvements were well above the significance level. Extremely good result was shown in the reduced need for the earlier applied blood pressure lowering medication, or even being able to quit these pills.

In my opinion the importance of the effect of C-peptide on the immune system, and through this on the whole body has a similar value as the great discovery of the stem cell therapies. Including the beneficial effects on endocrinological disorders, and as part of it the beneficial effect on carbohydrate metabolic diseases. These will be discussed in the next part.

Further investigations would be absolutely reasonable following these considerations, examining the beneficial effects of C-peptide on the immunological functions in detail, in the form of clinical trials

In order to achieve this good organization of the protocol is needed. Working out and introducing this requires hard work and keeping strict rules. It is highly important to make a critical analysis of the related literature. Without going into details I'd like to describe the four steps of working out the protocol:

a) Selecting the target issues: this is especially important is our situation, when the heterogeneous approaches outline the physiological – clinical correlations related to a certain professional field, immunology.

b) Working out the plan of the protocol: it is necessary to involve professional boards (including specialists) on one hand and creating working groups on the other hand. Their work needs to be refined through making agreements. It is also essential to make the competencies of each group clear. It is expedient to lean on randomize, control – possibly rely on international, multicentered - studies made in the field of work. There are some formal requirements (adequate volume, clearly set-up, uses adequate language, well structured, easy to handle) of the plan, besides the contextual ones. Defining the professional level of the coworkers gathering data is also a contextual condition.

c) The phase of evaluation: The plan should be sent out to a number of specialists (e.g. Korányi or the Immunological Centre in Pécs), where it is evaluated primarily concerning the fact, whether it is adequate to be introduced. Besides the clinical involvement, because of the upcoming issues of economic policy, it is worth considering inviting political partners, since they are directly affected.

d) Accepting the protocol, legitimization: following the proposal of the working group the professional board discusses, evaluates the professional quality, and – in case of acceptance – declares the protocol. Than the work following the protocol can start.

Endocrine diseases

There were 5 patients participating in the investigation.

Case	Age	Sex	Diagnose	Associated diseases
1.	35 years	female	Hypothyreosis	
2.	59 years	male	Hypothyreosis	
3.	48 years	female	Total thyreoidectomia	
4.	67 years	female	Total thyreoidectomia	
5.	50 years	female	Hypothyreosis	

Table 3. – The participants of the group of endocrine diseases

Evaluation according to the investigated aspects

Frequent tiredness: Ceased in each case (5 persons) due to the application of the spray.

Lack of appetite: Got better or ceased in the case of 2 persons, in 3 cases lack of appetite was not a typical symptom.

Weight gain despite of reduced intake: There was weight gain in 2 cases before applying the spray. Out of these in one case loss of weight (17,5 kg) happened, in the other case weight gain was no more typical. 2 patients indicated that there was no change in their weight after the treatment. 1 patient lost weight before applying the spray, which is a sign of hyperthyreosis.

Numbness of arms, legs: In the case of 3 persons decreased or ceased. In two cases this symptom was not typical.

Dry, itchy thick skin: In the case of 2 persons decreased or ceased. In two cases this symptom was not typical. There was no improvement in one case.

Constipation: In the case of 2 persons decreased or ceased. In 3 cases this symptom was not typical.

Hearing loss: In the case of 1 person it has improved, in 4 cases there was no hearing loss.

Reduced sexual desire: there is no change concerning this, since in 4 cases it was not typical before the treatment either, in 1 case it was reduced before and after the treatment as well.

Elevated cholesterol: In the case of 3 persons it decreased, in two cases it was not typical.

Depression: In the case of 1 person it decreased, in the other cases the typical symptoms were not there.

Somnolence: In the cases of 3 persons it ceased. In two cases it was not a typical symptom.

Freezyness: In all the 5 cases it has decreased or ceased.

Accelerated speech: In the case of 1 person it has accelerated after the treatment, in the other cases it was not typical.

Accelerated thinking: In the case of 1 person thinking has also accelerated. In the other cases it was not typical.

Swatting: In the case of 2 persons decreased or ceased. In 3 cases this symptom was not typical.

Infertility: It was a problem in 1 case, a 35 year old woman, there was no change after the treatment. The other 3 women were already after menopause, the 5th investigated case was a 59 year old man.

Miscarriage: One woman indicated miscarriage earlier, in the other 3 women there was no miscarriage.

Arrhythmia: In the case of 1 person it ceased, 1 person had tachycardia before the treatment as well, in 3 cases there was no arrhythmia before the treatment either.

Carpal tunnel syndrome: In the case of 2 persons it ceased, in 3 cases it was not diagnosed.

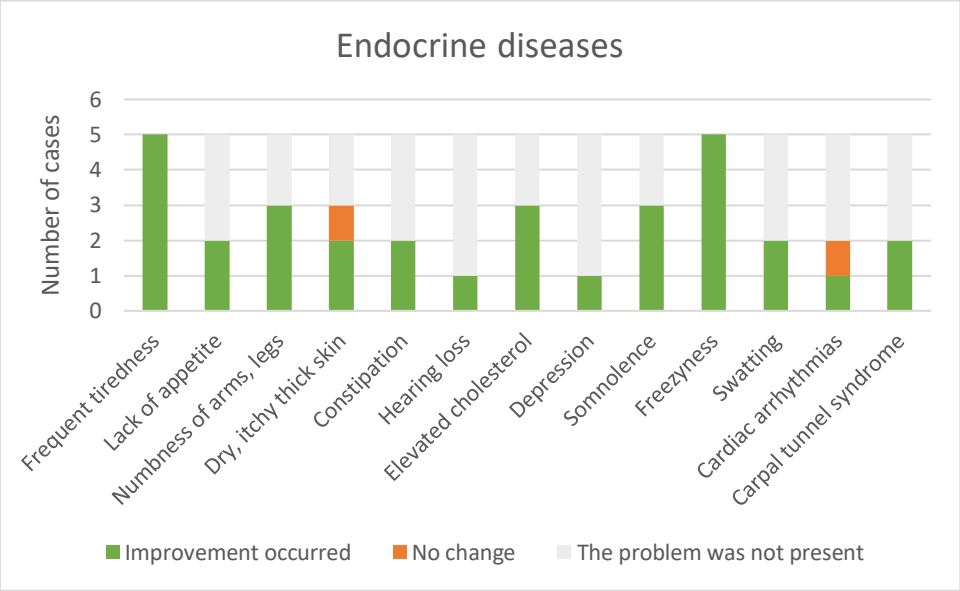

Figure 11. – Improvement of symptoms of endocrine diseases

Results of laboratory tests

TSH: During the period of our investigation there was no control laboratory test.

FT4, FT3: In the case of 1 person mild raise was noticed. In 1 case it was physiological before treatment as well. In 3 cases there was no control examination.

Anti – TPO: There are no data available to compare the values before and after treatment.

Thyroglobulin: In the case of 1 person it was negative both before and after the treatment. In the cases of 4 persons no control laboratory test was made.

Examinations with imaging technology

Cervical ultrasound: In 1 person the dissolvement of a 3 cm big lump was reported. In 4 cases there was no control ultrasound examination after the treatment.

Applied therapy: The patient, who lost 17,5 kg weight after the treatment, was able to stop taking 50 mcg Letrox.

Weight: The same patient lost 17,5 kg weight as it was indicated above.

Evaluation

In all cases tiredness and frezzyness ceased, that was frequent before the application of the spray. Those who had constipation before the treatment, reported that it ceased. The improvement was significant in the problem of lack of appetite, numbness of arms and legs, dry and itchy thick skin, constipation and somnolence. Swatting decreased in the same proportion, as well as Carpal – Tunnel syndrome ceased.

In one case the FT4, FT3 hormones raised moderately, and also speech and parallel thinking accelerated, and also in this case arrhythmia ceased. The other patient who lost 17,5 kg weight, got free of depression, and also this person was able to quit taking Letrox, which is a sign that thyroid functions became physiological.

Metabolic diseases

Nine patients were selected into this group.

Case	Age	Sex	Diagnosis	Associated diseases
1.	59 years	male	Diabetes mellitus type 2	
2.	35 years	female	Diabetes mellitus type 2	
3.	45 years	male	Diabetes mellitus type 2	
4.	38 years	male	Diabetes mellitus type 2	
5.	71 years	female	Diabetes mellitus type 2	
6.	52 years	female	Diabetes mellitus type 2	
7.	61,5 years	female	Diabetes mellitus type 2	
8.	51 years	male	Diabetes mellitus type 2	
9.	56 years	female	Diabetes mellitus type 2	

Table 4. – The participants in the group of persons with metabolic diseases

Evaluation according to the investigated aspects

Thirst: In the case of 6 persons thirst ceased, in one case it was not typical before the treatment either, in the cases of 2 persons thirst persisted.

Increased hunger: In the case of 3 persons it ceased, in one case it decreased. In 4 cases this symptom did not appear, in 1 case hunger persisted after the treatment as well.

Weakness: In the case of 5 persons it has decreased or ceased, in four cases this symptom was not typical.

Tiredness: In the case of 7 persons tiredness decreased or ceased, in 2 cases this symptom was not typical.

Weight: In the case of 1 person there was a loss of 13,5 kg weight, in 2 cases weight gain of 3 and 4,5 kilograms occurred. In 6 cases there was no change in their weight.

Loss of weight: The person, whose morning blood sugar level sank from 17,3 mmol/l to 5 mmol/l, lost 13,5 kilograms. In 1 case there was minimal loss of weight. In 7 cases this was not a characteristic symptom.

Numbness: In the case of 2 persons it ceased, in 2 cases it has decreased, in 5 cases this symptom was not typical.

Blurred vision: In the case of 2 persons it ceased, in 2 cases it has decreased, in four cases blurred vision was not a problem before applying the spray either. In 1 case low vision persisted.

Slow wound healing: In the case of 3 persons slow wound healing decreased, in 2 cases the time of wound healing remained the same. In 4 cases this symptom was not typical.

Frequent infection: In the case of 4persons it ceased, in 5 cases frequent infection was not a typical symptom before applying the spray either.

Dry skin: In the case of 1 person skin, in 1 case the problem of dry throat symptom decreased. In 6 cases this symptom was not typical.

Itchy skin In the case of 1 person the eczema ceased, in 8 cases this was not a typical symptom.

Irritability: In the case of 5 persons it has decreased or ceased, in four cases it was not a typical symptom.

Depression: In the case of 5 persons it ceased or it has decreased, in four cases this symptom was not typical.

Applied therapy: In 1 case the medication 2x270 mg Merckformin was not necessary any more, in 1 case the dosage could be decreased from 1000 mg to 500 mg. In 7 cases there was no information about the dosage after treatment.

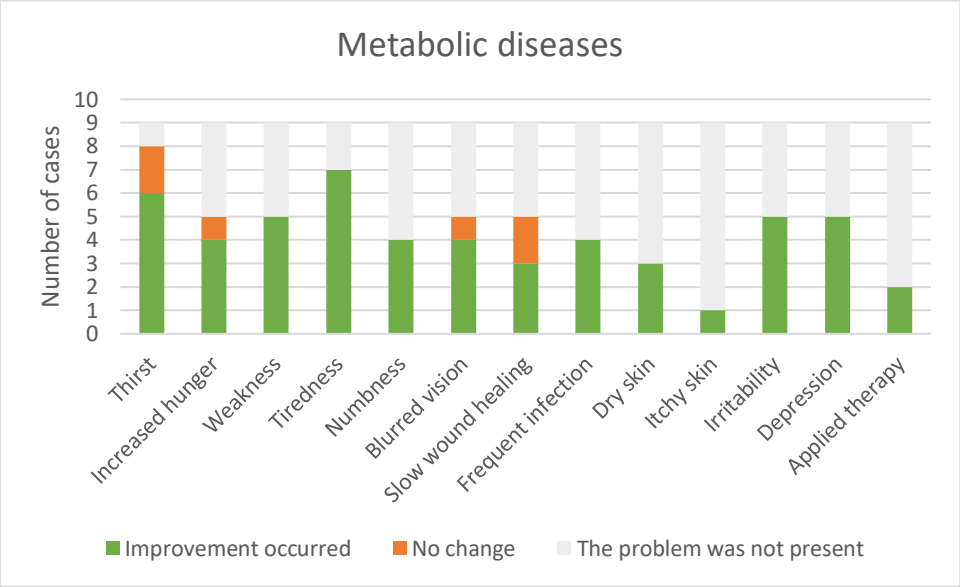

Figure 12. – The improvement of symptoms in metabolic diseases

Results of laboratory tests

Blood sugar: In 2 persons the values around 18 – 19 mmol/l sank to 5-8 mmol/l. In 7 cases there was no significant change.

HgbA1c: In 1 person during the application of the spray this value sank under 9%, which is within the normal range. In the other 8 cases there was no significant change.

The complication of kidney damage

Microalbuminuria: In the case of 1 person it sank to 2/3, in 1 case it didn't change, in 7 cases this complication did not occur.

Narrowed EGFR: In 1 person this value is narrowed, and it did not change. In 8 cases this complication was not typical.

Urea: In 6 cases there was no measurable change, in 3 cases this was not a typical symptom.

The complication of eye damage

Glaucoma: It is present in 2 cases, but there was no significant change during the application of the spray. In 7 cases the problem did not occur.

Retinopathia diabetica: In 8 cases this symptom is not typical, in 1 case it is.

The complication of nerve damage

Polyneuropathy: In the cases of 5 persons it ceased or decreased, in 1 case there was no significant change. In 3 cases this complication did not occur before the treatment either.

Numbness: In the cases of 5 persons it ceased or decreased, in 1 case there was no significant change. In 3 cases there was no numbness before applying the spray either.

Pain: In the cases of 3 persons it ceased or decreased, in 6 cases there was no such symptom

Vascular complications did not appear during the period of investigation, there was no need for amputation in the case of any patient.

Evaluation

After applying the spray there were the following significant changes:

Decrease in: thirst, increased hunger, especially weakness, tiredness and frequent infection. Furthermore numbness, blurred vision, slow wound healing also decreased. Dry, itchy skin became also less frequent.

Blood sugar: Laboratory test proved that the values sink to 2/3 in 2 cases, and so it became physiological. Out of these 2 cases in one case the percentage in HgbA1c measurement fell well below the acceptable range.

The complication of kidney damage: decrease in a microalbuminuria was proved in one case.

The complication of eye damage: there was no notable change by the end of the treatment

The complication of nerve damage: significant change was noticed in the assessment of polyneuropathy, numbness, and pain. Irritability and depression also significantly decreased.

Weight: In diabetes type 2 there is usually loss of weight due to the improvement of carbohydrate metabolism. This was specifically experienced in one case (13,5 kg loss of weight).

Applied therapy: In 1 case it was possible to quit medication, in 1 case the dosage of oral anti-diabetic medication was halved.

Infectious diseases

There are five persons in the investigated group.

Case	Age	Sex	Diagnose	Associated diseases
1	75 years	Male	Chronic Lyme Borreliosis	
2.	48 years	female	Chronic Lyme Borreliosis	
3.	65 years	female	Chronic Lyme Borreliosis	
4.	65 years	female	Chronic Lyme Borreliosis	
5.	43 years	female	Chronic Lyme Borreliosis	

Table 5. – Participants of the group of patients with infectious diseases

Evaluation according to the investigated aspects

Psychic aspects

Anxiety: In the cases of 3 persons it decreased or ceased, in the cases of 2 persons it was not typical.

Panic: In the case of 1 person it ceased, in the cases of 4 persons this symptom did not appear.

Exhaustion: In the cases of 3 persons it ceased, in the cases of 2 persons it was not a typical symptom.

Poor motivation: In the cases of 4 persons it was not typical, in 1 case it was a mild problem, and it has improved.

Changing mood: In the cases of 2 persons it has improved, in 3 cases it was not typical.

Depression: In the cases of 2 persons it has improved, in 3 cases it was not a typical symptom.

Irritability: In the case of 1 person it ceased, in 2 cases it decreased, in 2 cases it was not typical.

Frequent crying: This symptom was characteristic to 1 person, it ceased after the treatment, in 4 cases it was not a typical symptom. .

Early memory impairment: It has ceased in the cases of 3 persons, in 2 cases there was no significant change.

Disorganization: In the cases of 4 persons it ceased, in 1 case there was no significant change.

Difficulties with concentration: In the cases of 4 persons it decreased or ceased, in 1 case there was no significant change.

Forgetfulness: In the cases of 4 persons it decreased or ceased, in 1 case there was no significant change.

Difficulties with word finding: In the cases of 3 persons it became less frequent, in 2 cases there was no significant change.

Frequent slip of the tongue: In the cases of 3 persons it became less frequent, in 2 cases it was not a typical feature. .

.Using wrong words: In the cases of 2 persons it has improved, in 3 cases it was not typical.

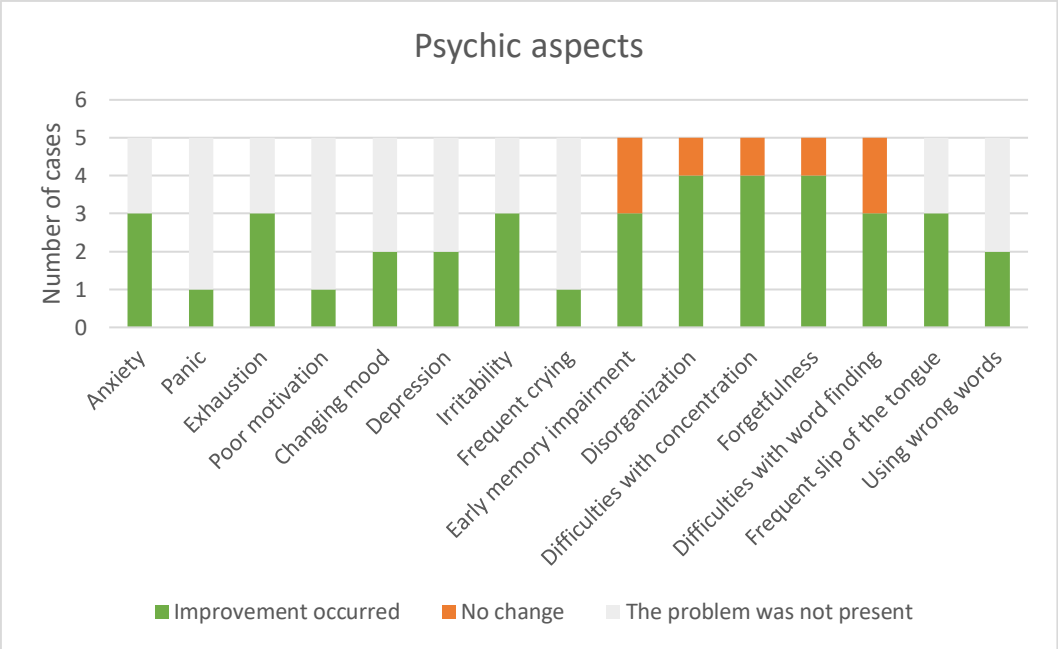

Figure 13. – Changes of psychic symptoms

Disorder of the connective tissue and locomotion

Clicking joints: In each of the 5 cases it has improved or ceased.

Tendonitis: It was not typical in our cases.

Pain at the insertion: In the case of 3 persons it became less frequent or ceased, in 2 cases there was no change.

Edema of the connective tissue: In the case of 3 persons it became less frequent, in 2 cases it was not a typical symptom.

Muscle tremor: In the case of 3 persons it became less frequent or ceased, in 2 cases it was not a typical symptom.

Muscle twitching: In the case of 3 persons it became less frequent or ceased, in 2 cases it was not a typical symptom.

Muscle weakness In the case of 3 persons it became less frequent or ceased, in 2 cases it was not a typical symptom.

Muscle cramp: In the case of 3 persons it became less frequent or ceased, in 2 cases it was not a typical symptom.

Muscle stiffness: In the case of 2 persons it became less frequent or ceased, in 1 case there was no change, in 2 cases it was not a typical symptom.

Bone pain: In the case of 2 persons it became less frequent or ceased, in 1 case there was no change, in 2 cases it was not a typical symptom.

Tenosinovitis: It ceased in the case of 1 person, in 4 cases it was not a typical symptom.

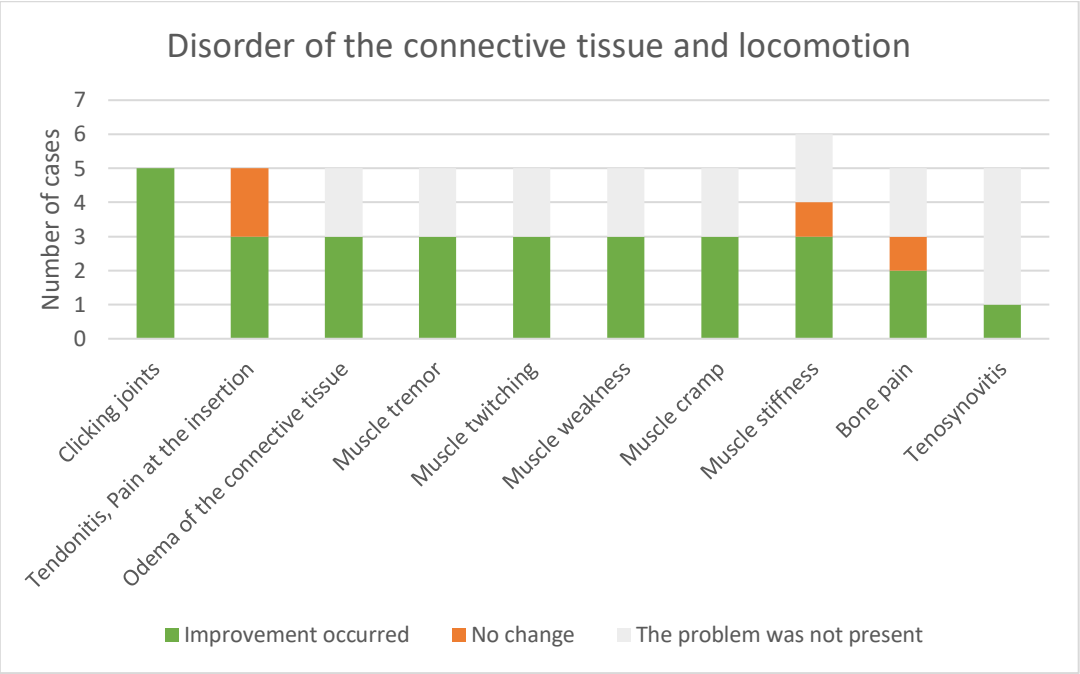

Figure 14. – Disorder of the connective tissue and locomotion

Abdominal visceral complaints

Frequent urination: In the cases of 2 persons it became less frequent, in 1 case there was no change, and in 2 cases this symptom was not typical.

Urine dripping: In the cases of 2 persons it became less frequent, in 1 case there was no change, and in 2 cases this symptom was not typical.

Gastrointestinal complaints: In the cases of 3 persons it became less frequent or ceased, in 2 cases this symptom was not typical.

Food intolerance: In the cases of 3 persons it became less frequent or ceased, in 2 cases this symptom was not typical.

Slow gut: In the cases of 2 persons it became less frequent, in 1 case there was no change, and in 2 cases this symptom was not typical.

Eructation: In the case of 1 person it has decreased, in 1 case it was rare, in 3 cases this symptom was not typical.

Hiccup: In the case of 1 person it has decreased, in 1 case it was rare; in 3 cases this symptom was not typical.

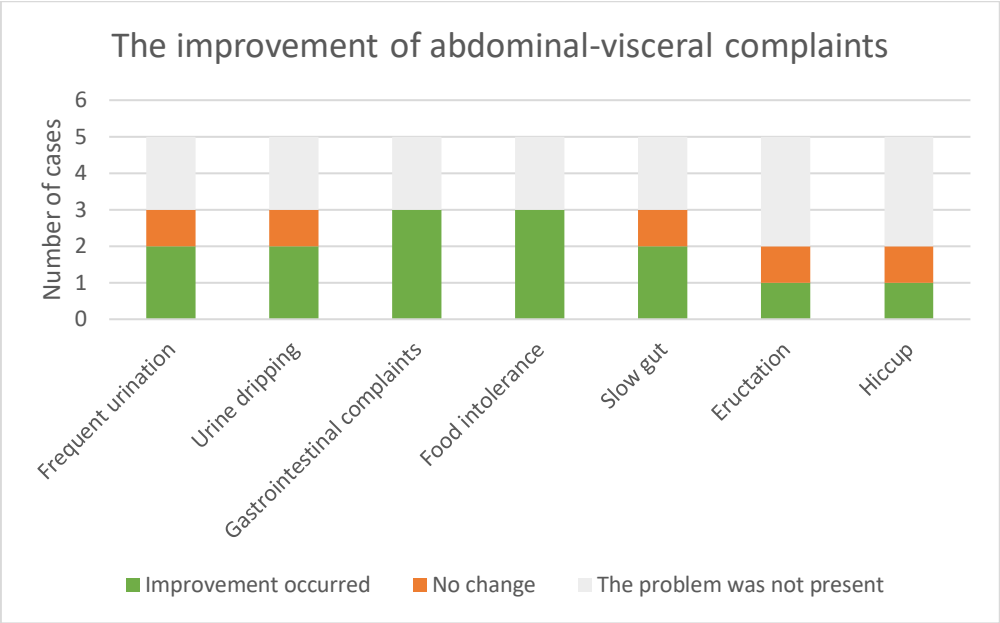

Figure 15. – The improvement of abdominal-visceral complaints

Complications and autoimmune disease patterns

Hyperaemic skin: It occurred in the case of 1 person, it ceased after applying the spray, and in 4 cases it was not typical.

Eczema, patches: In the case of 2 persons it ceased, in 3 cases this symptom was not typical.

Joint pain: In the cases of 2 persons it has improved, in 3 cases it was not a typical symptom.

Dry skin: It occurred in the case of 1 person, it ceased after applying the spray, in 4 cases it was not typical earlier either.

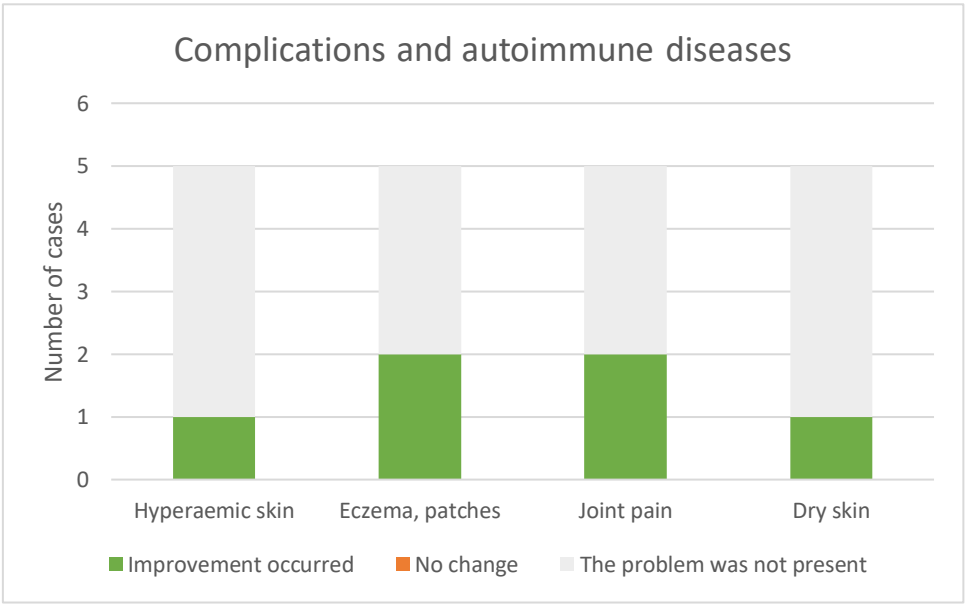

Figure 16. – Complications and autoimmune diseases

Cardiovascular disease

Arrhythmia: In the cases of 2 persons it ceased, in 3 cases it was not a typical symptom.

Hypertension: In the case of 1 person it ceased, in 1 case there was no significant change, in 3 cases it was not a typical symptom.

Hypotension: In the case of 1 person it ceased, in 1 case there was no significant change, in 3 cases it was not a typical symptom.

Fluctuating blood pressure: In the case of 1 person it ceased, in 1 case it has persisted, in 3 cases it did not occur earlier either.

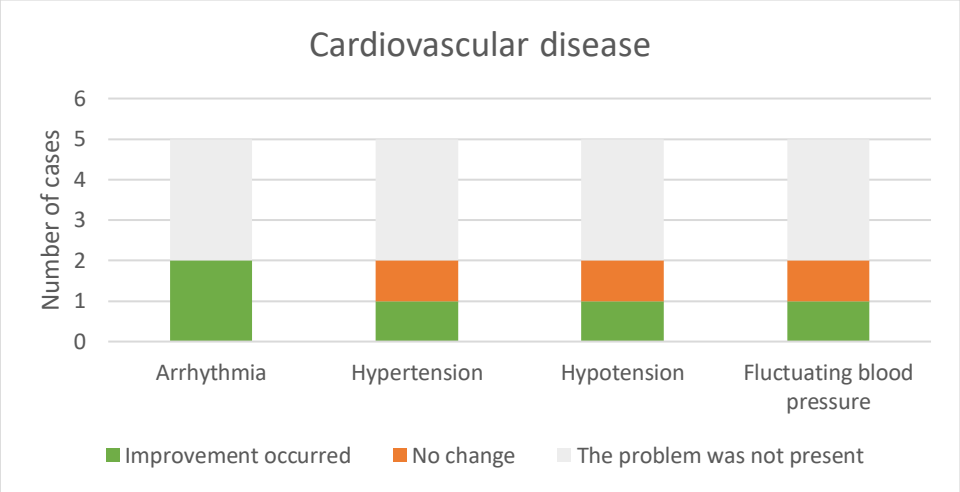

Figure 17. – The improvement of the symptoms of cardiovascular diseases

Complications of surgery

Stomach resection: 1 case

Thyreoidectomy: 1 case

Kidney stone crushing: once

Problems of diabetes and metabolism

Diabetes mellitus: In 1 case insulin resistance diabetes mellitus, which was arranged after treatment. In 3 cases there was no change in the physiological values. In 1 case it was fluctuating before treatment, but it was not measured again after treatment.

Endocrine disorders: In the case of insulin resistance (A. I.) the condition after thyroidectomy is balanced.

Malignant tumor: In 4 cases negative, in 1 case symptom free condition after breast carcinoma.

Diseases of the digestive system

IBS: In the case of 1 person it has improved, in 4 cases it was not typical.

Anorexia: In the case of 1 person it has improved, in 4 cases it was not typical.

Overweight: There was no significant change.

Coeliacia: In the case of 1 person there was no change, in 4 cases it was not typical.

Recurrent fever, inflammation, pain

Pain: It ceased in 1 case, it became less frequent in 4 cases.

Endocrine diseases

Insulin resistance: Improvement in 2 cases, in 3 cases it was not typical.

Hypothyreosis: In 1 case it was resolved, in 4 cases it was not typical.

Lyme test

Elisa: In 2 cases positive, in 2 cases negative, in 1 case not known.

Skull MRI

Demyelization nodules: Positive in 1 case

Use of aids

Hearing aid: in 1 case

Medical shoes: in 1 case

Evaluation

According to **psychic features** the greatest improvement appeared in the phenomenon of disorganization, difficulties in concentration, forgetfulness, difficulties in finding words and frequent slip of the tongue. The rate of improvement was 3/5, and 4/5. In the remaining feature this rate was 1/5 and 2/5.

According **to complaints of the connective tissue and locomotion** almost in each symptom the rate of positive change was 3/5 and 4/5. The only lower rate was 2/5 in the improvement of muscle cramp.

Abdominal, visceral complaints: Here the rate of improvement was 3/5 on average. There was an improved frequency in 1/5, 2/5 of the eructation and hiccup problems.

Problems of the immune system: These occurred only in 1/5, 2/5 of the cases.

Cardio-vascular diseases: The improvement was 1/5, 2/5.

Blood sugar, metabolism problems: The improvement was the same 1/5, 2/5.

Digestive problems: there was improvement in 1/5 of the cases.

Parkinson's disease, Sclerosis Multiplex, and Alzheimer's disease, and dementia, endocrine diseases: these were not present as associated disease of Lyme disease.

Recurrent fever, inflammation, pain: Decreased in each case or the complaints stopped, was not a typical feature.

Diseases

Neurological disease patterns

Sclerosis multiplex

The patients involved into this group:

Case	Age	Sex	Diagnose	Associated disease
1.	32 years	male	Sclerosis multiplex	Left hemisphere impairment
2.	49 years	male	Sclerosis multiplex	

Case #1:
Case #2:

Locomotion: muscle stiffness, spasticity decrease
Space perception improved
Tremor decreased
Speech: became more understandable and articulated
Constipation ceased
Sleeping: improved in both cases
Energy level: wake up well rested
Nervous system: reduced sensibility to light and sound stimuli
Short term memory improved

Central Paresis, Spastic paraplegia, Cerebral atetosis, Vigil coma, Commotio cerebri

Case	Age	Sex	Diagnose	Associated disease
3.	13 years	female	Central paresis	Congenital origin
4.	48 years	female	Spastic paraplegia	Asthma
5.	22 years	female	Cerebral atetosis	
6.	22 years	female	Vigil coma	Consequence of an accident, stroke, anomic aphasia.
7.	63 years	male	Commotio cerebri	Severe head injury due to an accident

Case #3: (Central Paresis) Reduced spasticity, speaks more in short sentences
Tone: more powerful
Choking (swallowing problem) decreased
Pupil reaction improved
Case #4: Spastic tetraplegia: no notable change
Case #5: Cerebral atetosis: sleeping and speech improved

Case #6: Vigil coma: no notable change

Case #7: Muscle tremor, spasticity decreased
Choking (swallowing problem) decreased
Initiates eye-tracking
Makes eye-contact
More alert

Traumatic Brain Injury, Meningoencephalitis, Epilepsy, Stroke, Thalamus ischemia, Encephalopathy ischaemica ,Paraparesis spastica hereditaria

Case	Age	Sex	Diagnose	Associated disease
8.	24 years	female	Traumatic brain injury	
9.	38 years	male	Meningoencephalitis	Somatomental retardation
10.	59 years	female	Epilepsy	Traumatic brain injury
11.	55 years	male	Stroke, Thalamus ischemia	Hypertonia
12.	64 years	male	Stroke	2.stroke, first in 2013
13.	21 months	female	Encephalopathy ischaemica	
14.	48 years	female	Paraparesis spastica heredi-taria	

Case #8: More intense
Cognitive functions improved
Starts understanding humor

Case #9: Speech improved a lot
Signals the need of defecation
More relaxing sleep
More patient
Susceptibility to infection reduced
RR values improved

Case #10: Frequency and severity of seizures decreased
Mood is better
Space perception improved
Irritability decreased
Temper improved
Speech disorder decreased
Cognitive functions improved

Case #11: Paralysis on the right side ceased in 3 days
Speech, walking, fine motor skills improved
Cognitive functions resolved

Case #12: Sleeping, mood improved
Ulcer on left foot improved due to local and intranasal C-peptide

Case #13: Increased muscle tone decreased
Lifts up head
Keeps head while lying on the stomach
Choking (swallowing problem) decreased
Tracking objects and sounds
Defecation got better, abdominal pain decreased
Sleeping improved

Case #14: Paraparesis decreased
Walking balance improved, can already ride the bike
Cool limbs, diarrhea decreased
Migraine less frequent

MSA-C, Alzheimer's disease, Parkinson's disease

Case	Age	Sex	Diagnose	Associated disease
15.	66 years	male	MSA-C	
16.	73 years	male	Alzheimer's disease	Prostate hypertophia, Diabetes mellitus
17.	72 years	female	Parkinson disease	Hypertension, Joint pain

Case #15: Tremor of arm and legs, imbalance decreased
Handwriting became legible, speech better articulated, more understandable
Incontinence of urine decreased
Nightmares decreased

Case #16: Due to the severe clinical condition only moderate improvement was possible in speech, mood and sleeping.
Diabetes became balanced.

Case #17: Walking improved.
Defecation got better.

Lissencephalia, Herpes encephalitis, RETT syndrome, Angelman syndrome

Case	Age	Sex	Diagnose	Associated disease
18.	18 years	male	Lissencephalia	Somatomental retardation, Lennox-Gastaut sy.
19.	7 years	male	Herpes encephalitis	Acute respiratory failure, Drug resistant epilepsy
20.	36 years	female	RETT syndrome	
21.	45 years	female	Sclerosis multiplex	Raynaud syndrome
22.	8 years	male	Angelman syndrome	Genetic origin, neurological symptoms, diagnosed at the age of 2,5 years

Case #18: Severely handicapped, bedridden, non-verbal, with a stomach-tube
Spasticity decreased, sleeping is better
Decubitus ceased after using the spray locally
Epileptic seizures are less frequent

Case #19: After treatment communicates with gestures and voice, tries to formulate words
Understands a lot of things
Improvement in eating manner
Coldness of limbs decreased
Sleeping cycle improved
Cooperative skills improved
Keeps eye contact, smiles more
Attention improved
Became more communicative

Case #20: Motor coordination improved, consistency of defecation physiological
Mood, attention, concentration improved.
Became more open

Case #21: Tiredness, numbness, tingle, muscle stiffness decreased
Stamina improved
Nocturia less frequent, than ceased
Constipation decreased
Sexual desire escalated
Joint and neuropathic pain became less frequent, muscle stiffness decreased
Sleeping got better, mood improved
Got 5 on the Sclerosis multiplex scale: late use of aid.

Case #22: Sleeping improved.
Defecation manner improved.
Susceptibility to infection reduced.

Autoimmune diseases

Morbus Chron, Raynaud syndrome

Case	Age	Sex	Diagnose	Associated disease
23.	72 years	male	Morbus Chron	

Case #23: Complaints of digestive functions decreased.
Tiredness decreased.
Better shape.

Cancerous diseases

Case	Age	Sex	Diagnose	Associated disease
25.	62 years	male	Brain tumor (malicious)	(glioblastoma)
26.	59 years	female	Face tumor	Hyperthyreosis, MRSA infection

Case #25: Hypotonia, tremor, imbalance improved.
Spasticity decreased, can sit unsupported.
Walks with help.
Weakness of limbs decreased, fine motor skills improved, can write again.
Expressed salivation ceased.
Incontinence improved, constipation ceased.
Mood, memory improved.
Speech and comprehension improved.

Case #26: Appetite, mood, digestion, sleeping improved.
Wound on the face clean, free of secretion.

MRSA infection

Case	Age	Sex	Diagnose	Associated disease
27.	55 years	female	MRSA infection	Hypothyreosis, Hypertonia
26.*	59 years	female	MRSA infection	Hyperthyreosis, Malignous tumor of the face

* This patient occurred also in the previous group

Case #27: After the applying the spray together with the Vargastem medicinal mushroom the chronic wound caused by MRSA became free of swelling, epithelization started.

Case #26*: There was a severe MRSA infection, despite of earlier antibiotic treatments the laboratory tests were positive for candida, after 6 weeks of treatment with the spray the wound exudate culture test was negative.

Psoriasis

Case	Age	Sex	Diagnose	Associated disease
28.	39 years	female	Psoriasis	

Case #28: There was no progression in psoriasis during the treatment. The skin is not itchy, there are signs of regression.

Migrain

Case	Age	Sex	Diagnose	Associated disease
29.	50 years	female	Migraine	
30.	59 years	female	Migraine	Hypertension

Case #29: After treatment the complaints of migraine moderately decreased.

Case #30: After applying the spray on the 6th day the patient became symptom-free. First during daytime, in a few weeks also the headaches at night ended.

Mood, memory, concentration, sleeping improved a lot.

Blood pressure became normal.

Diarrhea ceased as well, stopped losing weight.

Ear-nose-throat disease patterns

Auditory nerve damage, Otitis media chronica.

Case	Age	Sex	Diagnose	Associated disease
31.	9 years	male	Auditory nerve damage	Behavioral disorder, epileptic symptoms
32.	15 years	male	Otitis media chronica	

Case #31: After treatment there was no notable change concerning hearing ability.

According to associated diseases: attention, communication, mood, memory, numeracy improved.

Epileptic symptoms ceased. Respiratory infections less frequent.

Case #32: The symptoms in the lower respiratory tract caused by the chronic otitis media that has existed since early childhood, showed significant regression due to the application of the spray.

The clinical symptoms of the sinobrochial inflammation ceased. Parallel to this dull hearing also ceased.

In correlation with the sensory improvement his mood, attention, social abilities improved a lot. In connection with this his cognitive abilities also improved.

Musculoskeletal disease patterns

Artrogyposis, Shoulder joint pain, Joint pain

Case	Age	Sex	Diagnose	Associated disease
33.	11 months	female	Artrogyposis	Slow development
34.	50 years	female	Shoulder joint pain	Thyroid nodule, Hypertension
35.	77 years	male	Joint pain	

Case #33: During the application of the spray the volar reflected position of the left wrist started to improve, at present she can crawl.

Muscle hypotonia moderately decreased.

Case #34: The shoulder joint ligament bonds significantly decreased, range of motion increased. Now she is able to do exercises.

Can dress herself at ease.

Sleeping better

Case #35: Lower limb joint complaints decreased during applying the spray. He can already sit on his heels.

Sleeping better

Psychiatric diseases

Depression, Tentamen suicidi, Bipolar disorder, Panic syndrome

Case	Age	Sex	Diagnose	Associated disease
36.	53 years	female	Depression	
37.	44 years	male	Depression	Myoma uteri, Cysta ovarii, Hashimoto thyreoditis, Insulin resistance
38.	50 years	female	Depression	Panic syndrome
39.	30 years	female	Tentamen suicidii	
40.	52 years	female	Bipolar disorder	Panic syndrome, Hypothyreosis Meniere disease, Joint pain
41.	57 years	female	Panic syndrome	Hypertension

Case #36: Mood got better, depression decreased
Sleeps better, therefore more lively and active
Attention, concentration improved
Feels muscles more loose

Case #37: Mood swings stopped, sleeps better, wakes up more forceful
Concentration abilities improved
Ability to tolerate cold has improved, digestive complaints ceased
Weight, increased thirst decreased

Case #38: Sleeping, mood, concentration ability, difficulty in word finding improved
Tunnel feeling characteristic for panic syndrome decreased.

Case #39: Suicide urge ceased during treatment.

Case #40: Frequent, everyday cry ceased.
Sleeps through the night.
Apnea and cold limb feeling during panic ceased
Imbalance ceased, memory improved a lot. Therefore her performance increased.
Irritability to light and sound decreased.
Bipolar complaints as well as joint pain ceased.
Vision improved.

Case #41: Sleeping disorder decreased

Chronic tiredness syndrome

Case	Age	Sex	Diagnose	Associated disease
42.	61 years	female	Chronic tiredness	
43.	68 years	female	Chronic tiredness	Sleeping disorder

Case #42: Tiredness decreased, became more forceful

Memory, attention improved.
Constipation ceased.

Case #43: Tiredness decreased, sleeps better.

The effect of the use of C-peptide on the quality of life

Background and aims

An investigation was made among 91 persons using Vargapeptide, following certain clusters of problems, assessing parameters of internal medicine, neurology, special education, traumatology, social and psychological aspects. The question was, what are the type of diseases, inflammatory conditions, where the stimulation of the immunological state of the nervous system can achieve improvement, as well as what other effects can be described on the basis of valid results of examinations.

Method

In the investigation of the effectiveness of the C-peptide treatment, the participants and their close relatives provide the data and the reports about the experienced changes. The period of treatment was 1-18 months when recording data. Data were recorded in the frame of a personal interview between the participant and a staff member of the research group. The interview covered issues of the complex life-style and the changes in it, and also the effect on the family and the work environment.
When talking about psychic processes and the effects on the quality of life we include cognitive functions, memory, attention, concentration, state of operation skills, general arousal, level of motivation, mood regulation, anger and stress treatment, the effects of the quality of sleep, changes of the entire personality and the degree of mood disorders. We also monitored the state of emotional and social skills. Information was gained about this from the reports. The measurable changes, such as the desired loss of weight or blood pressure regulation assume causality.

The acquired, developed or congenital disease, impairment by all means becomes a definitive element of a person's personality and every day. It will continuously effect his/her environment in a mutual interaction. A simple flu can cause serious inconveniences, wound on the nose, being off from work, a canceled date. The permanent deterioration of health, the progressive or stagnant developmental disorder, impairments and complications on the basis of these, psychic and physiological consequences influence the person and his/her whole life in a complex way. In the same way it also effect, if the state of the person can be eased, improved, healed or developed even in the slightest degree. The support of persons with intellectual disabilities, autisms, multiple handicap happens through trainings, educational methods, behavioral therapies with the hope of a more livable life, or seeking the ideal balance, that everyone can reach the maximum potential compared to his/her abilities. In certain cases, such as immaturity of the nervous system, prematurity, the trainings can be effective, in other cases the underlying disease, the chronic pain has to be relieved, treated, and cured. There are permanent health damages, congenital conditions, where treatments help the stimulation, optimization of the existing, residual functions or aim at the regeneration of the cells, e.g. stem cell therapies. The most important when starting a therapy, treatment, medicine, is that we are aware in what field and in which period we can expect result. What are the primary and secondary, consequential effects? It occurs, that the improvement of the physical state results some more functional improvement, and this causes a better psychic state, which is a positive change that is measurable in the medical field as well. In the same way it may occur that coming out of a bad emotional state influences the physical state. When making pour investigation about C-peptide among the investigated users we focused on these changes. One thing that was a remarkable change

and effect, was the psychic improvement due to healing from physical symptoms and diseases. The other is the positive changes in the basic psychic functions, affecting the physical state, the behavior or certain skills. Sometimes these two take place parallel to each other. We need to be aware of what treatment means, what is healing and what is condition maintenance in certain situations.

The doctor, the therapist, the physiotherapist, the nurse, the psychiatrist, the psychologist, the teacher, the relatives help and see the changes in different fields, find different things important, see success in different ways, but their cooperation and consensus about the priorities is crucial. Each of them can have a reason to recommend C-peptide, and it depends on the results they can measure and notice, how effective they find it in the case of the target person. In the following we study the answers of the participants in the fields of the positive changes in psychic functions and behavior.

The effect of proinsulin C-peptid on persons with autisms and their families

21 persons from the participants of the investigation tried the Vargapeptide in order to lessen the symptoms of autisms. In the following we'd like to discuss the specific psychic aspects of persons with autisms and their families.

When studying and evaluating the effects of applying C-peptide in the cases of children with autisms spectrum disorder, it's worth taking those psychic aspects into consideration which influence the explanation and evaluation of the effects of the spray in the families of these children. In order to substantiate our discussion I'd like to highlight a few standing points about this topic.

The situation of families having a child with autisms differs from not only those families having a typically developing child, but also from those having a child another type of disability.

The specialty of autisms is that it is a pervasive developmental disorder, which means that the adverse development covers the whole personality. In other types of disabilities, such as physical disability, visual or hearing impairment, mental retardation, there is one function that is damaged and this has an influence – positive or negative – on other functions. For example a child with a physical disability may have problems with articulation, it may be hard to understand his/her speech because of the associated impairment of the speech organs, but may have outstanding visual abilities. Or visually impaired people often have piece movements but refined hearing function.

Autisms spectrum disorder is developmental disorder, which more-or-less covers each field of development. It is frequent to have a disturbed sleeping cycle; it is quite typical to have eating disorder, hypersensitivity, which causes that the child is frightened, anxious, scared of common things, that don't seem to be frightful for other at all. Also they may stick to habits inordinately, just to mention a few of the most common ones. These symptoms severely block the family life, as a system. Parents and siblings can't sleep well and enough because of the wakeful periods of the child at night. Due to the eating disorder of the child either the family members must eat monotonous food or the parent has to prepare several courses every day. The family can't go out or travel together, because the autistic child either won't enter certain places or if s/he is forced to do so, than disturbs everybody with his behavior which is so uncomfortable e.g. for the siblings, that they don't want to go out together any more.

There are certain cultural differences in different countries concerning the attitude towards people with disabilities. There is a slow positive change in Hungary, but it is still quite typical that people star at the disabled child, talk about him behind his back, make unpleasant inquiries from the parents about the child. Often there is a positive attitude towards children with other disabilities (physically disabled, visually or hearing impaired), or certain groups of children with intellectual disabilities, like children with Down-syndrome. The reaction is positive and kind in these cases, based on the feeling of pity and they find these children cute. The child with autistic behavior mostly feel uncomfortable in an unfamiliar environment, therefore encloses him/herself, isn't friendly and nice at all, and happens to rage, shout or cry. The reaction from the surrounding is either turning away from the family, leaving the scene, or even criticize or making comments.

The diagnostic criteria of autism is the joint presence of three main disorders: disturbed reciprocal social interactions, restricted communication and the problem of resilient behavior. This means in everyday life in a number of families, that the child refuses or hardly tolerates people except the narrow family members. Protests against the visit and presence

of strangers, which can cause such an unpleasant situation, that gradually the relatives, good friends stop coming to see the family. It is especially common, that the autistic child doesn't like being with other children of the same age, because he/she cannot understand their behavior, finds them often too noisy and irritating. Due to these it happens quite often that the parents become isolated, they break away from their friends, and they can hardly ever or never go to see them or receive guests. Their only company remains their autistic child, which can be depressing for the parents.

It is especially hard to find training, therapy and special educational intervention for children with autisms spectrum disorder in Hungary, and several times these provide limited success. There are few trained specialists, particularly in rural areas. These families often lose hope, because they can't see success of the gradual development. While in the cases of children with other disabilities often have a slow but in everyday activities noticeable improvement, in a lot of families with an autistic child it is quite typical to experience fluctuating development with relapses, which makes it even harder for the parents to be positive and optimistic.

The mother-child relationship and also the contacts with the other family members are often complicated and strange in the case of children with autisms spectrum disorder. A number of these children don't like being physically close to others (hugs, cuddles, kisses), refuse the common expressions of intimacy (waving, sitting in the adult's lap, etc.). Parents mostly experience the love of their child and create their ways to express it, but these often don't follow the accepted norms. This is not easy to experience many times, and it can be even more problematic to take it among others and make them understand the situation.
This is probably the reason why at the beginning of researching autism a theory was established that autism is a consequence of the mother's cold, rigid behavior. This fell shortly later, and professionals started to pay much attention to calm mothers, that the strange emotional relationship established with their child is not their fault.

The specificity described above often endangers the family with an autistic child both in financial and in emotional terms. In this situation even a small step forward may seem a huge progress. If the child has a sleeping disorder, even a few hours longer sleep, which provides the parents a longer quiet sleeping period, may be of great importance. The attention of the more restful, and quiet child can be attracted much more, and this can bring back a little hope for the development of the child. The lack of mental representations, that means the child with autisms disorder has difficulties or can't understand what's going on in the other person's mind or emotions, and this causes confusion, irritability and isolation.

General experiences gathered from the reports of the users

The investigated 91 persons, who tried the Vargapeptide because of their problems of internal medicine, endocrine or neurological diseases, showed the typical feed-back of a complex behavioral change, that accompanies the expression of basic functions and physical senses. This can be the regulation of defecation and urine and signing the need, expressing pain in the body, feed-back to their own physical needs, such as hunger, thirst, tiredness. The other big group of positive changes is better mood, expressing feelings, feed-back, cooperation, and the qualitative change of communication in the field of non-verbal interaction, vocabulary and expressive speech.

Also there are positive changes in appetite and eating, such as improvement of vitamin absorption, fluctuating blood sugar level, general health and fitness state. The stress around alimentation can decrease. All these elements can have an effect on the life of the target person, his/her family and people around him/her. Even a minimal ease of rigid habits gives back significant energy to the parents and care givers. Continuous opposition, keeping rules and routines takes away resources from the optimization of other activities and processes.

Swallowing and chewing are very important for independence, safe feeding. Chewing and the use of muscles inside the mouth contribute to the improvement of speech. The improvement of speaking abilities than influences the improvement of cognitive functions, thinking and ideation in a complex way. Psychic changes follow the physical ones in this case. But it is valid here as well, that the general level of arousal, the improvement of social skills gives a feed-back to the regulation and expression of vegetative functions.

Parents also report that their relationship with institutions has also improved. According to the parents' feedback, it is easier to connect to them that the number of everyday conflicts decreased. The mood swing of children and youngsters is reduced, their cooperative skills improve.

The behavior of the child becomes more understandable as his/her speech develops, mutual communication starts, the chance for cooperation is growing. Symptoms and the experienced changes of physical and mental state mix most often in the group of people with autisms. The most frequent improvement appeared in sleeping, which can lead to further positive changes both for the child and for his family. The child may become more alert, attentive, more recipient to initiatives, and the social restrictedness ca n ease through this. Relaxing sleep is extremely important for the family members.

The characteristic feature of autism is the developmental disorder covering several fields, therefore the symptoms; the improvement of the single functions cannot be separated. Improvement of speech can help socialization the child who slept and rested well may become less sensitive to stimuli that caused outburst earlier, the improvement of attention supports him/her to join in games and training activities. These changes and development primarily help the life of the parent, more and better sleep improves their well-being and they may have more time for their own activities.

<u>Symptoms and effects</u>

Sleeping disorder: tiredness, irritability, frustration
Disturbance of social abilities: isolation
Disturbed emotions, relationships, mentalization: difficulties in bounding, different bounding

In summary it can be stated that according to the reports the application of C-peptide brought significant changes in the symptom and the consequences of their disease for persons with autisms,

The changes of psychic features in the group of people with other investigated diseases

The WHO defined health in 1946 as “the state of physical, mental and social wellness”. Besides bodily and physical parameters the mental and emotional health, as well as the harmony of social relationships of the person is equally important. The experiences described in the study show that the effect of the proinsulin C-peptide was noticed by the participants and their family members in the improvement of physical parameters, as well as in the development of cognitive abilities and in the positive changes of psychic aspects.

In all cases of persons with hypertension lower blood pressure values were measured despite the quantity of blood pressure lowering medications could be decreased. The occurred changes in the other symptoms: end of dizziness, swatting, decrease of tiredness, less frequent head- and chest pain, ease of balance- and concentration problem can probably be summarized in the statement that the well-being of the patients improved. This certainly involves the raise of energy level, the decrease of disease awareness, better mood, which can achieve the optimization of relationships and life-style. It was reported that some people became more confident to start a change in their life-style, they started to feel the importance of doing sports and conduct healthy eating, because they experienced that their health can be controlled regardless to medicine.

In the cases of persons with endocrine diseases the authors of the study say in the summary of their evaluation: „in each case tiredness and fatigability ceased, which was frequent before applying the spray”, numbness of limbs and itchiness decreased. These changes clearly have a positive influence on the emotional state. Enervation, continuous tiredness is a disadvantage in the labour market, in social relationships and through this in the evolution of self-assessment.

Patients with diabetes reported the decrease of the earlier pathologically high blood sugar level, in 7 cases there was no change. The positive change appeared in a higher number of cases: feeling of thirst ceased in 6 from 9 cases, tiredness in 7 cases, ceased or decreased numbness and polyneuropathies, irritability and the tendency to depression in 4 cases.

In the group of patients with Lyme disease the largest scale improvements occurred in the field of psychic features. Out of the 5 investigated persons 3 or 4 indicated improvement in being disorganized, deconcentrated, forgetful, having problems in word finding and frequent slip of the tongue.

Also the patients with Lyme disease emphasized that they are able to start the day even early morning and work effectively without fatigue. This reacted to work, engagement in family life, doing sports, positive changes in body and appearance. In the long run the disturbances of attention and concentration caused low self-esteem in several cases, the improvement of these made the users more confident. Lyme disease is an acquired illness, and the consequences - losing certain skills and abilities, deteriorating health state - generate mourning and frequently secondary depressive processes. A spiral starts to develop, and the single medical treatments can only help a small part of it. The parents with this infection more or less learn to live with the cranked situation, but it always influences their psychic state. The pain, pain-killers, fatigue, the longer time needed to spend on resting, the narrowing social contacts all create a vicious circle.

Summary

Recently it is stated by researchers that mental and physical factors have not only the same importance in our health, but it is already declared that physical and mental health cannot be separated from each other.

Physical factors, physiological functions, self-knowledge, self-image, frustration, disease awareness all determine the quality of life, social and emotional relations, emotional state, earning capacity and lifespan as a whole in a complex way.

The participants of our investigation about the use of C-peptide reported improvement in their physical, mental and psychic state. Some of these changes are the consequence of concrete effects on the body, while other improvements are the secondary results of these effects. The complex effect should be underlined from the reports and descriptions. Decreased inflammation, ease of negative psychic states, higher level of activation and motivation, these can appear irrespectively from the concrete physical healing processes.

The end of pain and discomfort, the decrease of chronic disease awareness can belong to the improvement of physical symptoms. As a consequence of all these improvement of arousal, general health state, communication, mental abilities, cognitive abilities, social and financial situation can be experienced.

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List of figures

References

[i] Kwand-San Liu et al.: Insulin-related genes expressed in human placenta from normal and diabetic pregnancies In: Proc. Nati. Acad. Sci. USA Vol. 82, pp. 3868-3870, June 1985

[ii] Csajbok E.A. et al.: Expression of GLP-1 receptors in insulin-containing interneurons of rat cerebral cortex In: Diabetologia. 2019 Apr;62(4):717-725.

[iii] Anny H.X. et al.: Maternal Type 1 Diabetes and Risk of Autism in Offspring In: JAMA. 2018 Jul 3; 320(1): 89–91.

[iv] Thapa R. et al.: Reduced heart rate variability in adults with autism spectrum disorder In: Autism Res 2019 Jun;12(6):922-930.

[v] Brent Goodman: Autonomic Dysfunction in Autism Spectrum Disorders (ASD) (P5.117) In: Neurology Apr 2016, 86 (16 Supplement) P5.117;

[vi] Moshenets K. et al.: Heart Rate Variability in Patients with Type 1 Diabetes and Hypoglycemia with Different Control of Diabetes Mellitus In: Diabetes 2018 Jul; 67(Supplement 1)

[vii] Johansson BL, et al.: C-peptide improves autonomic nerve function in IDDM patients. Diabetologia. 1996;39(6):687-695.

[viii] Okamoto S, ez al.: Proinsulin C peptide obviates sympathetically mediated suppression of splenic lymphocyte activity in rats. Diabetologia. 2000;43(12):1512-1517.

[ix] Derkach KV, et al.: Intranasal Administration of Proinsulin C-Peptide Enhances the Stimulating Effect of Insulin on Insulin System Activity in the Hypothalamus of Diabetic Rats. Bull Exp Biol Med. 2019;167(3):351-355.

[x] Bazelmans T, et al. Heart rate mean and variability as a biomarker for phenotypic variation in preschoolers with autism spectrum disorder. Autism Res. 2019;12(1):39-52.

[xi] Aleksic M, et al. Signalling processes involved in C-peptide-induced chemotaxis of CD4-positive lymphocytes. Cell Mol Life Sci. 2009;66(11-12):1974-1984.

[xii] Lauterborn J.C. et al.: Cofilin Activation Is Temporally Associated with the Cessation of Growth in the Developing Hippocampus In: Cereb Cortex. 2017 Apr; 27(4): 2640–2651.

[xiii] Duffney LJ, et al. Autism-like Deficits in Shank3-Deficient Mice Are Rescued by Targeting Actin Regulators. Cell Rep. 2015;11(9):1400-1413.

[xiv] Siniscalco D,et al.: Inflammation and Neuro-Immune Dysregulations in Autism Spectrum Disorders. Pharmaceuticals (Basel). 2018;11(2):56.

[xv] Alhadidi Q, Shah ZA. Cofilin Mediates LPS-Induced Microglial Cell Activation and Associated Neurotoxicity Through Activation of NF-κB and JAK-STAT Pathway. Mol Neurobiol. 2018;55(2):1676-1691.