

# Deep Skills: Neuroenhancement and Synaptic Plasticity: The Neuroscience of Movement to Counteract the Effects of Covid 19

**Dario Furnari<sup>1,3,4\*</sup>, Letizia Pappalardo<sup>1</sup>, Elena Talyanova<sup>1</sup>, Melissa Delaney<sup>1</sup>, Susana Sanchez<sup>1</sup>, Khaled Hamlaoui<sup>1</sup>, Monika Milczarek<sup>2</sup>, Sebastien Lagree<sup>3</sup>, Sahara Jean<sup>4</sup>, Sergey Petrov<sup>5</sup>, Marey El hamouly<sup>6</sup> and Nadya Khan<sup>7</sup>**

<sup>1</sup>Department of Biomedical Sciences, Uk, Netherlands, Germany

<sup>2</sup>Department Monroe Medical, Uk

<sup>3</sup>Department of Lagree Studio, USA

<sup>4</sup>Department of Neuroscience, Australia

<sup>5</sup>Department of Lotus Academy, Ukraine

<sup>6</sup>Department of I.M.A.S, Switzerland

<sup>7</sup>Department College of Medicine and Health Sciences, United Arab Emirates

**\*Corresponding author:** Dario Furnari, Department of Neuroscience, University of Exeter, UK; Email: dariofurnari@hotmail.it

**Received Date:** July 22, 2020; **Published Date:** August 19, 2020

## Keywords

Neuroscience; Deep Skills; Recognition Memory; Spatial Memory; Physical Activity; Psychomotor Skills; Quantum Physics; Lagreefitness; Mental Health; Neuroplasticity; Cognitive Exercise; Massage; Exercise Physiology; Neurophysiology; Psychology; Psychophysiology

## Deep Skills: Positive Mind Neuroscience of Exercise to Counter Covid-19

### Memory and Learning in the Time of Covid-19

We must begin to lose our memory, even if only occasionally, to understand that memory is what fills our lives. Life without memory is not life. Our memory is our consistency, our reason, our feeling, even our action. Without her we are nothing.

Luis Bunuel

Memory is a wonderful mechanism, a means of transporting us back in time. We can go back a moment, or a large part of life. Sometimes not perfect, sometimes not authentic,

sometimes with nuanced details, memory is however the system that allows us to recall the information we have stored and learned from both the external and internal environment. It is the experience that changes us, the contact with the environment that changes our behavior through a series of structural and functional changes in our nervous system. The last challenge of neuroscience is precisely to better understand the complexity of these mechanisms and how complex phenomena such as learning and memory can occur.

Although the changes that occur within the individual brain cells can be relatively simple, considering that the brain is made up of many billions of neurons, the overall phenomenon is certainly very complex and makes the isolation and identification of the specific changes responsible of a certain really difficult memory. Similarly, although the elements of a specific learning task may be simple, its implications for the organism can be very complex [1]

From a neurobiological point of view, learning and memory are adaptations to the environment of the brain circuits that allow us to respond appropriately to situations we have previously experienced. Hence, learning (the process by

which the nervous system acquires new information and experiences) and memory (the ability to retain, retain and recall this information) represent the main mechanisms through which environmental events shape behavior. The experiences are not simply “accumulated” in the brain, but are capable of causing plastic modifications in our nervous system and of altering the circuits involved in our most sophisticated functions; in this way they change the way we act, think, perceive, plan. Although learning and memory are two closely related functions, they have temporal sequences and nervous mechanisms that do not always coincide. From a neurophysiological point of view, in fact, the learning process is essentially functional, ie entrusted to reverberant circuits and unstable morphological modifications, while the memory process is structural and presupposes stable morphological modifications. These changes are accompanied by an increase in protein synthesis and consist of an increase in the number and volume of the dendritic spines [2].

The importance of understanding the mechanisms that underlie the memory process, and the hope of being able to intervene when they are damaged, is therefore easily understood: they depend on the quality of life and the survival of the individual. This type of considerations helps to make the field of research on the mechanisms underlying memory particularly active. Many of these studies are carried out on animal models, but one wonders how much these studies are predictive of human reality both in terms of memory neurobiology (think, for example, of the different and more extensive development of the cortex in humans), and regarding the effect of drugs of potential therapeutic use in memory disorders. Some types of memory, however, have common characteristics in animals and humans, and animal models make it easier to study simple forms of learning and memory - such as the conditioned blink reflex - which are completely human similar to those studied in small mammals. Furthermore, the preliminary study on the animal very often allows to safeguard thousands of human lives and to avoid, for example, the experimentation of drugs on the ex-abducted man. Learning is the process by which experiences modify our nervous system and therefore our behavior. The primary function of the ability to learn is to develop behaviors suitable for a constantly changing environment. Experiences are able to change the way we perceive, act, think and plan. The ability of our nervous system to change in relation to experience is called synaptic plasticity and consists of a structural and functional change in the nervous structures which are reflected in changes in the processes of perception, memory, thought, planning and action.

### Learning Phenomena can be Distinguished in

- **Non-associative learning:** habit and awareness
- **Associative learning:** perceptual learning, stimulus

response learning (classical / Pavlovian conditioning), instrumental / operative conditioning by trial and error, motor learning, relational learning. Although the understanding of the mechanisms responsible for learning and other plastic modifications that take place in the adult brain still remains the subject of debate, there is broad consensus on the concept that at the basis of these phenomena there are modifications finely regulated by the strength of the synapses [3].

While in development, the changes are based on the reorganization of the connections that already exist between the cells, the strength of the synapses can also change in adulthood. The cellular mechanisms underlying these changes are constituted by transient modifications of the synaptic neurotransmission processes, while in the case of more lasting modifications they are constituted by changes in the processes of gene expression. Even after development is complete, the ability to change the organization of the nervous circuits of the cortex is not completely lost, but this ability decreases considerably (Bliss and Collingridge, 1993).

### Synaptic Memory and Plasticity

Synaptic memory and plasticity are studied in depth by neuroscientists who can count today on the use of different methodologies and technologies that range from behavioral studies to the investigation of gene expression. Thus understanding the changes in synaptic efficacy represents the most well-known field of investigation to date, even if memory is not just a succession of synaptic events. In a more holistic view of the process, memory is determined by the integration of multiple signals and activities that affect the brain sphere (attention, intention, interest, emotion), but also what involves the emotional state of the subject (hormonal structure, physical stress, etc.).

Recent data, obtained thanks to the development of morphometric techniques, underline how experience is also able to provoke changes in the morphology of the neuron and in particular of the synapse.

Three significant examples of morpho-functional alterations reported here were chosen.

A first example constituted by the demonstration that an environment rich in visual, auditory, tactile stimuli, etc., induces changes in the visual cortex level quantifiable as an increase in: a) weight and thickness of the cortex; b) size of the cell bodies of neurons; c) length and number of dendrites; d) diameter of synapses and dendritic spines; e) number of synaptic contacts of cortical neurons. These modifications can be induced in both young and middle-aged or old animals by suggesting that neuronal plasticity,

very pronounced in the developmental age, is maintained throughout life (Turner and Greenhough, 1985).

A second example is represented by changes in the hippocampal zone CA1, both in the number of neurons between synapses and dendrites and in the shape of the dendritic spines after induction of long-term synaptic enhancement (LTP) [4].

The third example of morpho-functional alteration is provided by the increase and decrease of pre-synaptic markers in neurons [5].

These different experimental observations clearly indicate how the storage processes are also related to morphological changes at the synaptic level as anticipated by the intuitions of Hebb [6] who proposed that if two neurons are active at the same time, the efficiency of the synapse is enhanced. Memory is a wonderful artifice of our central nervous system, capable of reconnecting us with our past. It allows us to go back a moment, or a long time. But what we know (or remember) is not perfect, it is a reconstruction of facts and experiences based on how we previously acquired them, and not how we would need them when we recall them. It is a reconstruction of the brain that differs from that formed by memory. Sometimes the details are lost but the essence always remains.

Memory is therefore the ability to consciously remember things that happened previously. The information is available for conscious recall and can be minuted and declared.

It is an extremely flexible type of memory that allows, for example, the display of the collision between two vehicles simply having heard the crash “crash”, through the recall of an experience that our brain has had in the past, but which has left track.

It is a mechanism common to all animal species and humans, which allows you to fix, preserve and recall experiences and information acquired from the internal and external environment, also derived from thought and emotions.

Through memory, man is able to reconstruct his own story, to organize himself and to project himself into the future. Memory creates our identity both as individuals and as people at the base of history and culture.

According to new neurophysiological theories, the secret of “becoming” lies in “communication”. Communication between men, through the word or non-verbal messages and communication between neurons, through the synaptic connections that intersecting and changing are able to adapt to new situations allowing change, the fulcrum of evolution.

## Anatomical Structures

Learning and memory are not functions confined to a single brain area or to a limited number of cells, but to different brain areas as already demonstrated by studies on rats with brain injuries carried out by the American psychologist Karl Lashley, in the first half of the 1900s, and by his pupil, Donald Hebb [6]. The latter's hypotheses stimulated the development of computer models of neural networks; his assumptions contributed to the study of memory, demonstrating that this information is not preserved in hippocampal structures and related diencephalic structures and that the cerebral cortex can be the main location for long-term storage of the different aspects of memory.

Since different cortical areas preside over different cognitive functions, it is not surprising that information relating to the specific cognitive function of the corresponding cortical area is stored in these regions [2].

## Hippocampus

Although different areas of the brain play a role in the consolidation of different forms of learning and memory, the hippocampus has been recognized as having a vital role in particular in the formation of declarative memory, such as semantic and episodic memory. In 1957, Scoville and Milner observed that bilateral removal of the hippocampus, as a treatment of epilepsy in the H.M. patient, caused anterograde amnesia. Since then, several studies were conducted and the specific role of the hippocampus and temporal lobes in memory formation was explicitly identified.

The hippocampal formation, whose shape resembles a sea horse, is a specialized region of the limbic cortex, located in the temporal region, folded and curved to assume a complex three-dimensional shape. Its bark has only three layers instead of six, therefore it is archicortex. It is formed by: uncus, dentate gyrus, corpus callosum, fornix, toothed fasciola, hippocampal sulcus, hippocampal gyrus and collateral sulcus. The entorhinal cortex channels most of the neo-cortical afferents and efferences to hippocampal formation thanks to neurons that relay the incoming information to the granular cells of the dentate gyrus through a bundle of axons, known as the “perforating path”.

Subsequently these neurons send axons into the CA3 field of the same hippocampus. The terminations of the fibers coming from the dentate gyrus form synapses with the dendritic spines of the pyramidal cells of the CA3 field: an axon heads downwards, out of the base of the pyramid, while a long and thick trunk heads outwards upwards. This dendrite and its ramifications are dotted with 30,000 dendritic spines. These spines are the site of structural and biochemical changes

responsible for the synaptic plasticity phenomena known as long-term potentiation (LTP).

The axons of CA3 pyramidal cells branch out in two directions. A branch ends in the adjacent CA1 field, where it forms synapses with dendritic spines of other cells, the other branch travels along the fornix to reach structures of the basal midbrain, including the septum and mammillary bodies. Another axon system connects the CA1 pyramidal cells with their counterparts on the opposite side of the brain.

Pyramidal cells CA1 provide primary hippocampal efferences: they send axons to neurons in the subicular complex, whose axons subsequently project out of the hippocampal formation, to the entorhinal cortex and, through the fimbria, to the basal midbrain.

With these assumptions and with today's neuroscientific evidence, we can say that the complexity of the pandemic situation in which we find ourselves is already reshaping our brains. We must rediscover our deep skills, those related to our empathic ability, to know how to be with others, to listening, to solidarity, but also to morality and responsibility. These positive strategies will have positive effects on our perception of the disease and its course and, consequently, will have beneficial effects on the restructuring of our synaptic connections. Like good psychotherapy.

Through a plethora of attitudes and lifestyles that we can put into action during the quarantine we can be the actors and protagonists of our destiny in a positive sense: avoiding "binging" with negative news, replacing them with reading or listening through audio-books of works of literature, poetry, the use of interactive systems via the web to view archaeological sites, art galleries, but also listening to classical music, good conversations via Zoom, WhatsApp, Teams and other means, the possibility of going outside to walk, getting used to a silence full of positive experiences, indulging in the kitchen or gardening, or in any hobby capable of diverting our attention to the pandemic, all this and much more, it can contribute positively to preventing and re-establishing those neurochemical and electrical balances of our brain. As far as the control of emotions is concerned, the best strategy from the point of view of neuroscience and therefore of the brain is to activate "prefrontal" mechanisms, that is to activate a very anterior part of the brain that is involved in short-term memory tasks, working memory, planning, strategy, problem solving. Neuroplasticity and irisin are, in my opinion, the two main components acting as important stimuli during physical movement. They provoke an increasing in the functions of the brain, thus improving cognition and behavior, as well as a prevention of obesity and diabetes, which are a serious risk in our society, being a public health crisis that affects most of the Western civilization.

The ongoing global epidemic of chronic non-communicable diseases (NCDs) is related to changes in lifestyle, including low physical activity (PA) levels. Physical inactivity is a major public health challenge and has been defined as the fourth leading cause of death worldwide. The health benefits of regular PA are well established, and elimination of physical inactivity would remove between 6 and 10% of NCDs and increase life expectancy. Moreover, cardiorespiratory fitness (CRF) is a strong predictor of health and longevity. There are large individual differences in CRF among adults who are sedentary and who have a history of not engaging in regular exercise.

Recent neuroimaging studies also suggest that a combination of omega-3 fatty acids, aerobic exercise and cognitive stimulation prevents a decline in the gray matter volume of the frontal, parietal and cingulate cortex in patients with mild cognitive impairment. Particularly interesting are those studies suggesting that physical activity, a balanced diet, cognitive stimulation or the management of conditions such as diabetes and obesity are preventive factors in Alzheimer's diseases.<sup>20</sup>

## Neuroplasticity

Neural plasticity is the ability of the nervous system to change its function. The above quotation synthesizes the main notion about the relationship between the importance of offering as many stimuli as possible to our brain, especially during the first years of life, because, in so doing, we give infants and young children the chance to develop a series of important notions that will regulate their future life forever. Our program of physical exercise, through music and instructions, has the aim to stimulate, through the sensory system, the plasticity of the brain and cognition while constructing a well-balanced psychological and social attitude. Teaching PE to young children, who are still trying to know the structure of their body and how to use it, so, to control and organize their movements according to a project, can be very effective: "Control of movement is highly adaptable to changing demands and that is a result of neural plasticity being turned on. ... Training can increase motor skills. ... We may call this learning but it is in fact a matter of neural plasticity because activation of the skills does not involve conscious recall as does memorization of telephone numbers. We have often heard about Coronavirus and its effects on the brain in recent weeks. In fact, the neural tropism of this virus (SARS-Cov-2) is an emerging and extremely important topic to consider in these months of global lockdown.

For months, silence, isolation, the desert of our cities, the solitude of our monuments have become our existential "storm". Deafening silence, a sense of bleak emptiness, physical and emotional paralysis, fear and bewilderment are

some of the perceptions and feelings that do not leave our nervous system indifferent. And how could they not? How do all these stress factors not already affect our brain?

That SARS-Cov-2 in itself has neurological effects is evidence that is emerging with increasing force and that is being investigated by specialists all over the world: the journal *Neurology* has issued a specific call on the subject and on PubMed under the heading "COVID-19 nervous system" numerous studies appear. We already know that this virus attacks the receptors for the sense of smell from the earliest stages of the disease, i.e. those nerve endings responsible for transmitting the impulse and the odorous message from the periphery of our sense organs, especially the nose and mouth, to the brain.

Now, if on the one hand the coronavirus itself attacks the nervous system and therefore the brain itself, on the other hand, numerous epigenetic factors that are stressful from isolation, imprisonment, fear, etc. have the ability to negatively reshape our brain function.

## Psychomotricity: Through the Game and the Psyche Improve the Immune System

### Psychomotricity-Introduction

Psychomotricity can be defined as the set of those motor behaviors that express certain aspects of the person's psyche. Psychomotricity is a discipline that is based on the principle of man understood as the mind unit body: the person is the result of an inseparable union of the mind with the body, components that are they influence each other in their manifestations. The execution of a movement is conditional therefore from the emotional, affective, social components that characterize the personality of man and in turn, motor activity influences the emotional-emotional area, the cognitive area, the organic area, the social area.

It was the French neurologist E.Dupré who coined the term in the early twentieth century psychomotricity and to enunciate the so-called law of psychomotricity: it foresaw a development parallel of motor functions, action skills and psychic functions. From that period onwards psychomotricity had a remarkable evolution in contents and a widespread application in various fields that we can subdivide into: re-educational, therapeutic, educational.

### Psychomotor Re-Education

The first psychomotor address is the re-educational one, which it has the objective is to recover the psychomotor gaps accumulated in the various age groups, from childhood to old age.

### Psychomotor Therapy

A second orientation is the therapeutic one which, addressed in particularly to all subjects with relational affective problems, it aims to restructure, through motor activity, behavior in relation to the world of others. Relaxation techniques or autogenic training are often used for this therapy.

### Psychomotor Education

It can be defined as a set of theories and methods operating that carry out an educational action through the mediation of the body. According to French Pierre Vayer, one of the most authoritative leaders of psychomotor skills, education

### Psychomotor is based on the Following Stages Which Include:

- The discovery of one's self
- The relationship between one's self and the world of things
- The relationship between yourself and other people

What constitutes for Vayer the pivot of the educational action during childhood is the structuring of the body pattern.

Among the most representative scholars of psychomotricity is Jean Le Boulch who, for his eclectic training (physical education teacher, doctor and psycho-pedagogue) has elaborated interesting and original educational theories followed by valid operational proposals.

### The Body Scheme

The body scheme is the awareness of one's body in relation to the external world in the spatial and temporal dimension.

The notion of body scheme is the result of long studies that have led neurologists, psychiatrists and psychologists questioning the perception of the body understood as awareness of one's self. IS' an image of the human body that corresponds to the mental picture we make of our body.

The body pattern, which we can also define body image, is structured from 0 to 12 years and is restructured from 13 years until the end of the person's life.

### Stages of the Structuring of the Body Scheme

1. Stage of the lived body
2. Stage of the lived body
3. Stage of the perceived body
4. Stage of the body represented

## Psychomotor Rehabilitation

Psychomotor reeducation is mainly aimed at pathologies of neurological origin, psychiatric and behavioral behavior of the child.

It is indicated both in cases of disorders attributable to organic causes and to causes psychic disorders that occur mainly through tonic, motor and ed functions emotional and creating difficulties in the control and use of psychomotor functions, in relationships and learning.

### These disturbances refer to:

- Psychomotor Pathology
- Psychomotor retardation
- Language delay
- Psychomotor instability
- Awkwardness
- Clumsiness
- praxic disorders
- Disturbances in the organization of the body scheme
- Disturbances of the space-time organization
- learning difficulties (dysgraphies, dyslexias)
- Neural Injury
- Mental Insufficiency
- Psychiatric Pathology

Psychomotor re-education is accomplished through the action of the body, creating situations in which motor skills, sensory, tonicity, cognitive and affective functions are solicited globally, through various techniques that use relaxation, play, drawing etc, for the purpose of help the child to organize his activities in the most suitable way to establish relationships with the world, to achieve maximum autonomy according to its means, to affirm its own personality and identity.

## Psychomotoric Rehabilitation in Postural Rehabilitation

If we carefully observe a man who is in an upright position we can see how he rests on a small base, while the maximum width and the maximum circumference of his body resides at the level of the shoulders and hips. The support base, with united and parallel feet, is delimited by a line that connects the toes and the heels and laterally passes along their margins. This base widens a little if we slightly spread the tips. For these considerations the human body in this position can be compared to a truncated cone with the minor base resting on the ground. You can easily verify the poor stability of this position if you stand with your eyes closed and in an upright position and with feet together; after a certain time there is a sense of staggering which is corrected with a muscular effort that makes the position safe. As soon as one foot is brought forward, that is, widening the support base,

one is again secure and firm. Our standing is therefore not as natural as it would seem at first glance. A fleeting glimpse into the animal kingdom shows how almost all vertebrates living on earth walk on four limbs; only in running do they move one or two limbs off the ground for a very short time. We too build four-wheeled wagons, tables and chairs with four legs. A two-wheeled wagon or bicycle must therefore fight to achieve balance. Man with his two limbs has the same balance problems.

So, next to structural determinants (nervous structures and sensory receptors) there are psycho-emotional, environmental, experiential and socio-cultural determinants which, in intimate connection with each other, determine the perceptive activity of the subject and his behavior and orientation environment. Perceptual activity represents the point of contact of the individual with reality: our behavior is adapted to reality as it is perceived by us at all times. The individual does not react to an absolute and incontrovertible reality, but to his perception of reality: the perceptual field thus becomes the reality itself for the individual. Body reality is no exception: the ego lives and acts its own body and how it perceives it, with all the emotional and sensory and motor values. Regarding the latter, we must always keep in mind, as Schilder reminds us, that "there are no perceptions without actions"; therefore a body pattern cannot be structured except through adequate perceptive - motor; active or passive activity; on the other hand, no motor function can be recovered without simultaneously recovering the relevant scheme. There are many useful proposals in this regard, which can put the subject in a condition to develop a significant gnostic-perceptual process, where necessary by resorting to appropriate facilities: respiratory re-education exercises, both active and passive segmental mobilization, lateralization, balance, sensorimotor coordination, space-time structuring, as well as postural rehabilitation exercises (see for example Picq and Vayer, 1968; Le Boulch, 1979; Loudes, 1980). In addition to movement, it is necessary to keep in mind the importance of "non-movement": relaxation. Together with the relaxation techniques proper, such as Autogenic Training (Scoppa, 1990), Jacobson's Progressive Relaxation, respiratory techniques, it is necessary to underline the usefulness of those therapeutic proposals which in general favor a reduction in the state of chronic muscle tension by freeing the body. from parasitic and dysfunctional contractures. For this purpose, the effectiveness of the Bioenergetic Analysis techniques (Traetta, 1998; Scoppa and Borrello, 1998) are emblematic, which lend themselves well to being integrated with more strictly physio-kinesitherapy and biomechanical methods for a truly holistic approach (Scoppa, 1996, 1999a, 1999b, 1999c). The basis of these therapeutic proposals, aimed at reducing the state of chronic tension in the body, lies in the fact that the ability to become aware of the body

and to elaborate the body pattern are seriously hampered by the muscle-tension state and emotional tension. This clinical evidence also finds experimental confirmations (Ruggieri et al., 1983), which have documented in this regard how the degree of body self-perception is inversely proportional to the level of myographic tension.

## Body Relaxation Techniques: Wintrebert Method

### The Stress

It is the body's response to stimuli of any nature (emotional, but also microbial, toxic, traumatic, thermal ..) which would tend to worsen the functional balance of the body. Stress is therefore a beneficial event which, if limited in time, helps us to adapt better to changes in the environment around us. When, on the contrary, the unbalancing events are continuous, symptoms can be produced which worsen the quality of life. Connected to stress can be persistent tachycardia, neck and back pain, headache, urticaria, unmotivated anxiety, insomnia, increased cholesterolemia, excessive sensitivity to cooling diseases, disorders in the sexual sphere.

Relaxation consists in releasing the muscles through different techniques, relaxing the mind and body from time to time.

It allows you to decrease tension and find balance, a state of well-being. According to the technique used you can relax some parts of the body, some groups of muscles or the whole body. If you have had the opportunity to experience forms of relaxation, you will know the physical, psychological and emotional beneficial effects that this brings. You have no doubt perceived in the body the pleasure of relaxation, as well as the resulting sense of psychological calm. In fact, relaxation is a truly effective tool for restoring and maintaining a state of harmonious balance.

### Relaxation Occurs Physiologically With:

- Slowing of the respiratory rate
- Reduction of oxygen consumption
- slowing of the heart rate, decrease in blood pressure
- Decrease in tone and peripheral musculature etc.

### On a Psychological Level, Relaxation Occurs Through:

- Feeling of tranquility and relaxation
- Decrease in supervision
- Indifference towards internal and external stimuli etc.

In Psychomotricity the techniques used are manifold, from listening to music to guided imaginations, from psycho body contact, to the use of contact with mediating objects,

to motor-muscular relaxation techniques such as the progressive relaxation of Jacobson, Wolpe, Wintrebert, to Autogenous training (lower cycle).

### Guided Imagination

The imaginary is a powerful drug, as it helps us to overcome anxieties, fears, moments of depression and also becomes a valid support to communicate better in all circumstances of life. This type of imaginative technique is supported not only by music, but also by breathing exercises, self-relaxation, concentration and inner listening. Difficulties may arise when viewing images, especially at the beginning. This is due to the fact that the images can represent aspects of oneself or situations that are the cause of malaise and discomfort. And the mental barriers that we often build serve to prevent us from going deep when we are not ready to do it. Visualization exercises are particularly suitable for achieving a state of relaxation by listening to appropriate music accompanied by an imaginative visualization exercise it allows us to slow down our vital rhythms, to improve the perception of our body which, little by little, becomes able to "feel" the passage from the state of malaise to that of well-being.

### Jacobson's Progressive Relaxation

It is a technique based on alternating contraction / relaxation of some muscle groups. It was conceived in the thirties by the American physician and psychologist physiologist Jacobson. The technique was born from the desire to quickly dissolve states of tension, anxiety or stress and is also suitable for people who are unable to practice autogenous relaxation, meditation or other techniques.

### Schulz Autogenic Training

Method experimented by the Berlin neurologist Schulz in 1932, it is a relaxation technique that allows you to release daily tensions and recover vital energy.

It is a method of self-relaxation that allows you to loosen psychic and physical tensions, and allows, through complete control of your body, to achieve a high level of psychic relaxation and achieve spontaneous changes in muscle tone, vascular function, respiratory activity, cardiac and internal organs.

The practice consists of a series of body positions and self-convincing sentences. Schulz defined the method, a method of self-relaxation that allows you to modify psychic and somatic situations. "Training" means training, that is, gradual learning of a series of exercises designed to achieve the neurovegetative balance, continually undermined by states of tension, anxiety and stress. The word "autogenous" that means.

## Neurophysiological Notes

Speaking of relaxation, the importance that it has on the tonic function cannot be overlooked, but to understand this, it is necessary to mention some notions of neurophysiology. For a more detailed study of the topic, the reader is referred to the bibliography of this work.

Muscle tone is a minimal contraction present in all muscles: at rest; it increases when the subject is in stress conditions. The functional area that allows the adjustment of the tone is the reticular formation. The latter represents a very important crossroads, consisting of ascending and descending fibers, which allow the transmission of a large number of stimuli, connecting the spinal motor neurons and the brain integration centers. From the activating ascending way of the reticular formation depend the states of consciousness ranging from coma to alert consciousness. It also regulates the vegetative life. Due to its characteristics both as a meeting and reception station for various stimuli from the periphery of the body, and as an activator, it is able to produce behaviors ranging from a generic activation state to an alert state.

From a phylogenetic point of view, brain structures can be divided into three systems with different time of appearance in human history: the spinal cord system, which is the oldest and presides over reflex or unconscious activities, the paleo encephalus, which it is less ancient than the previous one and presides over the functions that involve the activation of emotional states; and the newer brain, the most recent, which presides over higher cognitive and associative processes. The reticular formation is part of the paleo encephalon, the structure used to activate emotions. This, together with its crossroads characteristics of numerous stimuli at the start and arrival, explains why, by regulating muscle tone, a change in anxiety responses and more generally in the intensity of emotional states is determined by the return effect.

Relaxation can thus educate to self-control, it can reduce stress and consequently improve the immunological function of our body and allow an increase in EEG theta rhythms, which are present in the dream state of consciousness.

The neurophysiological phenomena examined allow us to explain how relaxation has become a real therapeutic tool, intended for those subjects suffering from anxiety, some psychosomatic disorders, stress and children with speech disorders such as stuttering, echolalia, difficulties of self-control and, therefore, to children with mental and motor disabilities.

The main tools used by me, specific to Functional Psychomotricity in this psychomotor path and in the

specific case in Covid's disease, are: motor-muscle relaxation techniques (Wintrebert and Jacobson), the Le Bon Depart method, the Orlic method, the Psychocontact®, Communicational Tonematics®, and Gestational Kinetic Dynamics®.

Muscle-motor relaxation techniques are methods for breaking down tension states, as they help to cope with internal conflicts, emotional-affective dissatisfactions, mistrust related to one's psychosomatic function, feelings of weakness and tiredness; subjects who express widespread discomforts with rhythm-respiratory-kinetic disorders, who have little knowledge of their body pattern, poor attentional skills and easy fatigue, all issues that can be found in a subject with Covid-19.

Complete relaxation of the muscles acts both on the neurophysiological side and on the whole person, who returns to establish a tonic dialogue with herself on the experiences and meanings of the body as a place of tonic-emotional and relational experiences. The purpose of these methods is to make the person feel comfortable in his body, overcoming instability and inhibitions that pervade him, and achieving self-knowledge and awareness, an ability in the interpretation of proprioceptive sensations, an improvement in attentional skills and spatio-temporal organization, and therefore a better awareness of the body scheme.

All this, through these techniques, which are muscular and psychic experiences, a remarkable psychoemotional balance is achieved; it is therefore a help intervention that uses body mediation to expand and reactivate the communicational. Another relaxation method is the gestural method Le Bon Depart, which working on the graphic sign, on the association rhythm-melody-space and on the exercises on the sand cushions, favors the development of the body scheme, of the spatial and temporal organization, of the motor and graphic execution. In this way, in addition to relaxation, we have an integration of the body image, due to the various experiences of imitating gestures and all the exercises of decontraction, to an improvement of the spatio-temporal orientation, which translates into a better auditory perception, muscle, and visual and therefore a better balance and tonic control; Finally, it is also a method of preparation for writing and its application is very important on the motor skills of the hand the Orlic.

It is a gesture education technique, consisting of a series of exercises and set in 3 moments: 1-self-awareness, 2- self-structuring and integration, 3-self-expression and social integration. What the method expresses is an organizational-motor process to improve the person's potential, skills, and availability; favoring a personological, psychophysical and socio-relational growth, improving psychoemotional balance, giving the body its importance.

In the Communication Tonematics, on the other hand, posture and voice are harmonized with codes with different communicative meanings, linked to an interpretation of a way of being, of existing and of representing oneself, expressions of self declared through the voice with creative dynamism. It is about honing the skills of all those functions that participate in phonation; In this way, the Kinesthetic perception is enhanced, the mobility and effectiveness of the movements of each organ that participates in synergistic relation to mobile vocal production is improved. With psycho-contact, the needs and defenses of the subject are brought up to date and allow the shapes of conflicts to be dissolved). The skin represents the body boundary and the Psycho-contact is a method that manages to overcome this boundary, creating a relationship with the external way through a tactile dialogue that fixes the stimulations that reach the subject and consolidates the internalization of the body fencing, allowing the passage from the unconscious to the conscious body scheme for a better relational openness of the subject; in this way a Conscious Body System is built for a better evolutionary path of the person.

### **Lagree Method: Besides Fitness, Natural Steroids to Defeat a Virus**

LaGree Fitness™ takes the foundations of Body Building, focused on strength, and mixes them seamlessly with a work of muscular endurance and intense cardio training. The Megaformer offers constant endurance and endless exercise options; allows the body to switch quickly and uniformly from one exercise to another to allow a constant increase in heart rate. LaGree Fitness™, ultimately, allows you to burn more fat and improve body composition thanks to the greater intensity that derives from the integration of strength training and cardio training.

In order for a training method to be effective, it is important to train at a considerable intensity. The body needs to reach a certain threshold of exercise intensity in order to be stimulated to change and adapt. Only with intense training can excellent results be obtained. LaGree Fitness™ is a total body workout. All muscle groups are strengthened in a non-aggressive way, without stress, it is an intense workout for the muscles and delicate for the joints. The vertebral column remains protected, the mind is busy, and the body pushed to its limits. This workout uses the time available to speed up the metabolism, burn fat and improve body composition. LaGree Fitness™ focuses on form and every movement is kept within the range of set goals.

LaGree Fitness™ equipment is adjustable to allow you to work on different muscle groups. It works with slow and controlled movements. None of the exercises are performed using momentum.

When working with and against resistance slowly, the tension on the muscles remains constant, recruiting more muscle fibers. Slow and controlled movements activate the muscle fibers that burn fat. Each set is performed for at least 60 seconds to stimulate both fast and slow-twitch muscle fibers. Transitions are kept to a minimum to keep muscle work and heart rate high.

To start seeing the first results on your body, simply train three times a week with LaGree Fitness™. No further training sessions are needed for the client. Each LaGree Fitness™ class lasts 40 to 55 minutes depending on the study and the instructor. They call it Pilates under Steroids, and it is a new training technique that has been developed by Sebastien Lagree and that is depopulating in the United States.

It is a method of teaching and practicing Pilates that sees the use of a particular machine, called Megaformer, which would be able to move even more muscle bands simultaneously, bringing the training to a higher level.

In particular, the classes of this type of Pilates last about half an hour and, according to the creator of the method, in thirty minutes a student will have the opportunity to experience a workout related both to toning and aerobic type.

The studies that are joining this new fitness model are increasing in the United States, as it seems that the results are truly amazing and can be noticed in an even shorter time range than just Pilates.

### **The Physical Exercise as a Countermeasure**

Sports and immune defenses in the time of coronavirus  
The ability to fight pathogens, such as viruses, depends a lot on the reaction capacity of our body. To defend ourselves effectively you need to be well, be healthy, strong, resistant and have a properly functioning immune system.

There are numerous scientific studies that highlight a positive influence of physical activity on the immune system, especially if practiced constantly and without excess. In fact, it is known that regular physical activity, with the right duration and intensity, helps improve the body's immune response.

Sportsmen tend to run a very low risk of contracting infections or exposing themselves to infections, compared to people who do not play sports. Quarantine or hypokinesia brings: reductions in muscle mass, in the mineral content of the bones and in the cardiovascular ability to regulate blood pressure. In addition, there is an increased risk of postural hypotension accompanied by neuro-vestibular dysfunction which can lead to problems while staying completely at home.

This consideration has led scientists to seek adequate countermeasures.

**One of the proposed countermeasures is:**

THE PHYSICAL EXERCISE to increase the immune system or better PREVENTIVE AND ADAPTIVE MOTOR ACTIVITY. There are two mechanisms by which regular training helps the immune system, the first is a short-term mechanism: exercise is believed to help the immune system to identify the pathogens to neutralize; the second mechanism is long-term: regular exercise slows down the natural aging process and the progressive reduction of the immune defenses it entails.

Turner and Campbell had dealt with the relationship between exercise and the immune system themselves, one of the points that most interested them (and it is the main focus of this article) is the very common assumption that it is true that exercise moderate strengthens the immune system but on the contrary very intense exercise would lower the defenses. To be more precise, the prevailing theory states that intense physical activity opens a "window" of lowering the immune system immediately following the activity during which you are most subject to infections.

Research data indicate that even a single maximal exercise can induce a temporary increase in plasma volume and sensitivity of the arterial receptors responsible for monitoring blood pressure, which allows the maintenance of  $VO_2$  max.

In addition, greater attention must be paid to the design of devices that allow effective resistance training as a means of maintaining muscle function. According to Covertino, devices with an eccentric component could be important because, with eccentric actions, muscles and bones can be subjected to a greater load.

**Training against greater resistance could also serve to maintain the calcium content in the bones that support body weight. Total body circuit training five times a week:**

There will be a circuit from Monday to Friday which will consist of muscle exercises with postural exercises done on the fitball or with a tilting table for proprioceptive exercises; as an alternative to the latter, the vibrating platform will be used;

Before carrying out the circuit, it is important to carry out a functional warm-up as regards the regulation of body temperature and heart rate, in addition to the fact that cold can cause injury.

In this way, 5-10 minutes of normal speed exercise bike will be carried out.

After the second time, a 5-10 minute cool-down of the exercise bike is carried out as the initial warm-up but a little less intense and at the end, in order not to have the muscles contracted, muscle stretching is recommended: thighs - calves - back - shoulders - triceps - neck.

Muscle stretching will be carried out gradually by holding the stretch position for 5 initial seconds to gradually reach the sensation of stretching; after these 5 you do 20 seconds, without springing, but keeping the degree of tension without feeling pain but only tension!

It is important to do this before training as a precaution to injuries to initially stimulate the muscle that is cold and not very elastic, and repeated at the end of the training so as not to contract the muscle that has just worked.

## How Massage Eliminates Toxins Caused by Stress

Massage is applying pressure or vibration to a part of the body, or successively to the whole body; objectives may be the good feeling, and/or to heal injury, improve circulation and relieve tension in the muscles or skin.

Due to the body contacts between the practitioner and the client or patient, some massage parlors provide more sexually oriented services (see erotic massage). It is not always obvious in advance whether a massage parlor provides authentic non-sexual massage by licensed practitioners or is actually a front for erotic massage or prostitution. However, establishments which offer erotic massage services usually provide hints at the services offered using a variety of innuendos, such as "VIP massage" or "full service". These innuendos are noticeable by their absence at establishments providing only therapeutic massage. Where massage is used for its physical and psychological benefits, it may be termed remedial massage therapy.

## The Massage Session

Most massage techniques involve the client being treated lying down on a massage table. There are a few exceptions: see Thai massage, below, for an example. Due to the necessary body contacts between the practitioner and the client or patient, care is taken to avoid inadvertent sexual arousal. Although the massage subject is generally unclothed, their body is "draped" with towels or sheets. This also helps keep the subject warm. Areas of the body such as the areas around the groin and intimate parts of the body are normally not touched at all in therapeutic massage.

The treatment normally starts with the client face down for the first part of the session, and they then roll over for the

second part of the session, which is carried out face up.

### Types of Massage

There are well over 150 different types of massage therapy. Various styles of massage have developed from a number of sources.

#### Swedish Massage

This style utilizes long, flowing strokes. Pressure is mainly applied on the skin level. The main purpose is for relaxation by pushing around or kneading the muscle groups. Oil, cream, or lotion is applied on the skin to reduce friction and allow smooth pushing and pulling of the tissues. This style of massage is generally attributed to the Swedish fencing master and gymnastics teacher Per Henrik Ling (1776-1839).

#### Trigger Point Therapy

A trigger point is an area of a muscle that refers pain sensations to other parts of the body. Trigger Point Therapy applies pressure to these points leading to immediate release of tension and improved muscular functioning. This work is based upon the trigger point research and manuals of Dr. Janet Travell.

Sometimes this work is incorporated into other styles of massage therapy such as neuromuscular therapy (NMT).

#### Deep Tissue Massage

Pressure is applied on the muscles in order to reach deep muscle groups. It is allegedly effective for sport injury. The drawback is the surface pain afterwards resulted from pressing the skin too hard. Usually only a minimal amount of lubricant is used on the skin.

#### Chinese Tui Na Massage

Chinese massage that is similar to Zhi Ya, but more on pushing, pulling and kneading the muscle.

#### Chinese Zhi Ya Massage

Chinese massage based on acupressure. It is similar to Tui Na massage except more on pinching and pressing at acupressure points.

#### Shiatsu

Japanese massage based on acupressure. It is uncertain whether it originated from Chinese Zhi Ya.

#### Scalp Massage

In some barber shops in Hong Kong, scalp massage often lasts 30 minutes to 45 minutes during shampooing of the hair.

#### Sole or Foot Massage (also known as Reflexology)

This is generally practiced by the Chinese, as some believe that each spot on the sole of the foot corresponds to an

internal organ. The theory supposes that an ailment of an internal organ will be associated with the nerve ending on the sole of the foot.

Before the massage, the patient's feet are soaked for about ten minutes in a foot bath, typically a dark colored of hot water and Chinese herbs. The massage therapist uses liberal amounts of medicated cream, to moisturize the foot and to provide lubrication. The knuckles on the therapist's hand are usually used to provide a hard and smooth implement for the massage. As pressure is applied to the sole, theory holds that a healthy patient should not feel any strong pain. Painful spots, reflexologists believe, reflect illnesses of other parts of the body. The practitioner rubs and massages the painful spots to break down rough spots and accumulated crystals and increase circulation.

The ailments are healed when the sore spots of the sole are treated and removed by massage. Based on this theory, some shoe liners are made with pressure points to stimulate the soles of the feet to promote better health of the overall body. The nature of these "crystals" has yet to be elucidated or demonstrated scientifically. Regardless of the actual correlation of reflexology to internal organs, many enjoy it for the mix of stimulation and relaxation.

#### Ancient Thai Massage

This is often called passive or assisted yoga and is usually soothing because of its emphasis on stretching and loosening the body. It is also known as Ancient massage because its roots go back far into history, originating in India and then becoming popular in Thailand.

The patient changes into pajamas and lays on a firm mattress on the floor. (It can be done solo or in a group of a dozen or so patients in the same large room.) The practitioner leans on the patient's body using the forearm to apply firm rhythmic pressure to almost every square inch of the patient body. No oil is applied except sometimes to the patient's palms and soles. A full course of Thai massage lasts anywhere from one to two hours including pulling fingers, toes, ears etc., cracking the knuckles, walking on the patient's back, arching the patient's back in a rolling action etc. There is a standard procedure and rhythm to the massage. Sometimes in a large group massage, the practitioners do the procedures in unison.

Thai massage is a tourist attraction in Thailand and the practitioners are usually women. In some establishments, they sit inside a room with a large display window, so clients can pick the girl they like by the number tag on them. Some say the young and pretty women usually give a poor massage because of lack of experience. A full massage in Thailand costs around US\$17 (in 2001) depending on exchange rate

and location (it may cost ten times more inside a five star hotel).

### MA-URI Massage

In its focus on health and healing, on personal empowerment and growth, MA-URI is a modern expression of an ancient medium. It was introduced and given name in 1990 by Hemi Hoani Fox and forever after this medium has been revealing new pathways and deeper layers of meaning through the combined efforts of Hemi and Katja Fox of the MA-URI Institute. It has its roots in ancient Polynesian principles that focused on a dynamic and creative approach to life where you developed the skills of mastering all aspects of your life. It uses basic Hawaiian Lomi-Lomi Nui dance movements to facilitate the energy flow within the body and the mind. Through the power of intent and breath these movements are then intensified by a Maori focus on action and effectiveness, accelerating a new range of movement not just within the physical body, but also within beliefs, memories and emotions, within relationships, finances and job situations. Licensure, in an effort to demonstrate their knowledge. Over 25 U.S. states currently use it as a requirement for their state license as well.

### Conclusions

A realistic strategy to deal with the situation is to supply our body with all those molecules that science has shown to be able to strengthen the immune system. In fact, it is known that optimal immunocompetence depends on the nutritional status and the deficiencies of micronutrients - as well as unbalanced diets, can reduce the defenses against infections.

There is a bidirectional interaction between nutrition, infection and immunity:

The immune response is compromised if nutrition is insufficient, predisposing people to infections, and at the same time. A poor nutritional status can be aggravated by the immune response itself to the infection.

The resistance to infections can therefore be improved by dedicating attention to the contribution of some micronutrients - with respect to which deficiency can be found, especially in some phases of life (elderly and children) - and to an optimal, that is, varied and balanced diet. Add to this an adequate physical and psychomotor exercise, a positive state with a relaxed mental attitude and with positive thinking through meditation or other psychocorporeal techniques. Neuroscience also deals with this

### References

1. Carlson NR (2002) *Fisiologia del comportamento*, Padova.

2. Gasbarri A, Tomaz C (2005) *La Memoria. Aspetti Neurofisiologici*.
3. Madison DV, Malenka RC, Nicoll RA (1991) Mechanism underlying long-term potentiation of synaptic transmission. *Annu Rev Neurosci* 14: 1379-1397.
4. Chang FF, Greenhough WT (1984) Transient and enduring morphological correlates of synaptic activity and efficacy change in the rat hippocampal slice. *Brain Res* 309(1): 35-46.
5. Bailey CH, Chen M (1983) Morphological basis of long-term habituation and sensitization in *Aplysia*. *Science* 220(4592): 91-93.
6. Hebb DO (1949) *The organization of Behaviour: A neuropsychological theory*, Wiley, New York.
7. Choi DW (1988) Glutamate neurotoxicity and diseases of the nervous system. *Neuron* 1(8): 623-634.
8. Chow VW, Mattson MP, Wong PC, Gleichmann M (2010) An Overview of APP Processing Enzymes and Products. *Neuromol Med* 12(1): 1-12.
9. Cirrito JR, Kang JE, Lee J, Stewart FR, Verges DK, et al. (2008) Endocytosis is required for synaptic activity-dependent release of amyloid-beta in vivo. *Neuron* 58(1): 42-51.
10. Citron M (2004) Beta-secretase inhibition for the treatment of Alzheimer's disease--promise and challenge. *Trends Pharmacol Sci* 25(2): 92-97.
11. Clader JW, Wang Y (2005) Muscarinic receptor agonists and antagonists in the treatment of Alzheimer's disease. *Curr Pharm Des* 11(26): 3353-3361.
12. Cullen WK, Suh YH, Anwyl R (1997) Block of LTP in rat hippocampus in vivo by beta-amyloid precursor protein fragments. *Neuroreport* 8(15): 3213-3217.
13. Cummings J (2010) What can be inferred from the interruption of the semagacestat trial for treatment of Alzheimer's disease? *Biol Psych* 68(10): 876-878.
14. Dawson GR, Seabrook GR, Zheng H (1999) Age-related cognitive deficits, impaired long-term potentiation and reduction in synaptic marker density in mice lacking the beta-amyloid precursor protein. *Neuroscience* 90(1): 1-13.
15. Dineley KT, Westerman M, Bui D (2001) Beta-amyloid activates the mitogen-activated protein kinase cascade via hippocampal alpha7 nicotinic acetylcholine receptors: In vitro and in vivo mechanisms related to

- Alzheimer's disease. *J Neurosci* 21(12): 4125-4133.
16. Dineley KT, Bell KA, Bui D, Sweatt JD (2002) Beta-amyloid peptide activates  $\alpha 7$  nicotinic acetylcholine receptors expressed in *Xenopus* oocytes. *J Biol Chem* 277(28): 25056-25061.
  17. Dominguez DI, De Strooper B (2002) Novel therapeutic strategies provide the real test for the amyloid hypothesis of Alzheimer's disease. *Trends Pharmacol Sci* 23(7): 324-330.
  18. Duncan AJ, Heales SJ (2005) Nitric oxide and neurological disorders. *Mol Aspects Med* 26(1-2): 67-96.
  19. Fehér A, Juhász A, Rimanóczy A (2009) Association between a genetic variant of the  $\alpha 7$  nicotinic acetylcholine receptor subunit and four types of dementia. *Dement Geriatr Cogn Disord* 28(1): 56-62.
  20. Fezoui Y, Teplow DB (2002) Kinetic studies of amyloid beta-protein fibril assembly. Differential effects of  $\alpha$ -helix stabilization. *J Biol Chem* 277(40): 36948-36954.
  21. Finckh U, Kuschel C, Anagnostouli M (2005) Novel mutations and repeated findings of mutations in familial Alzheimer disease. *Neurogenetics* 6(2): 85-89.
  22. Fodero LR, Mok SS, Losic D (2004)  $\alpha 7$ -nicotinic acetylcholine receptors mediate an A $\beta$ (1-42)-induced increase in the level of acetylcholinesterase in primary cortical neurones. *J Neurochem* 88(5): 1186-1193.
  23. Gandy S (2005) The role of cerebral amyloid beta accumulation in common forms of Alzheimer disease. *J Clin Invest* 115(5): 1121-1129.
  24. Ghirardi M, Casadio A (2002) Le basi molecolari neuronali e molecolari della memoria. *Le Scienze* (dossier "La memoria")14: 4-11.
  25. Giuffrida ML, Caraci F, De Bona P (2010) The monomer state of beta-amyloid: where the Alzheimer's disease protein meets physiology. *Rev Neurosci* 21(2): 83-93.
  26. Grassi F, Palma E, Tonini R (2003) Amyloid beta (1-42) peptide alters the gating of human and mouse  $\alpha$ -bungarotoxin-sensitive nicotinic receptors. *J Physiol* 547(1): 147-157.
  27. Haass C, Schlossmacher MG, Hung AY (1992) Amyloid beta-peptide is produced by cultured cells during normal metabolism. *Nature*, 359(6393): 322-325.
  28. Hardy J, Selkoe DJ (2002) The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *Science* 297(5580): 353-356.
  29. He W, Barrow CJ (1999) The A beta 3-pyroglutamyl and 11-pyroglutamyl peptides found in senile plaque have greater beta-sheet forming and aggregation propensities in vitro than full-length A beta. *Biochemistry* 38(33): 10871-10877.
  30. Huber G, Martin JR, Löffler J, Moreau JL (1993) Involvement of amyloid precursor protein in memory formation in the rat: an indirect antibody approach. *Brain Res* 603(2): 348-352.
  31. Ishida A, Furukawa K, Keller JN, Mattson MP (1997) Secreted form of  $\beta$ -amyloid precursor protein shifts the frequency dependence for induction of LTD, and enhances LTP in hippocampal slices. *Neuroreport*, 8(9-10): 2133-2137.
  32. Kamenetz F, Tomita T, Hsieh H, Seabrook G, Borchelt D (2003) APP processing and synaptic function. *Neuron* 37(6): 925-937.
  33. Kastin AJ, Pan W (2008) Peptides and Hormesis. *Crit Rev Toxicol* 38(7): 629-631.
  34. Kendig EL, Le HH, Belcher SM (2010) Defining hormesis: evaluation of a complex concentration response phenomenon. *Int J Toxicol* 29(3): 235-246.
  35. Kuo YM, Emmerling MR, Vigo-Pelfrey C (1996) Water-soluble A $\beta$ (N-40, N-42) oligomers in normal and Alzheimer disease brains. *J Biol Chem* 271(8): 4077-4081.
  36. Laird FM, Cai H, Savonenko AV (2005) BACE1, a major determinant of selective vulnerability of the brain to amyloid-amyloidogenesis, is essential for cognitive, emotional, and synaptic functions. *J Neurosci* 25(50): 11693-11709.
  37. Levey AI (1996) Muscarinic acetylcholine receptor expression in memory circuits: implications for treatment of Alzheimer disease. *Proc Natl Acad Sci USA* 93(24): 13541-13546.
  38. Levin ED (2002) Nicotinic receptor subtypes and cognitive function. *J Neurobiol* 53(4): 633-640.
  39. Lopez-Toledano MA, Shelanski ML (2004) Neurogenic effect of  $\beta$ -amyloid peptide in the development of neural stem cells. *J Neurosci* 24(23): 5439-5444.
  40. Loo DT, Copani A, Pike CJ (1993) Apoptosis is induced by beta-amyloid in cultured central nervous system neurons. *Proc Natl Acad Sci USA* 90(17): 7951-7955.
  41. Lowenstein CJ, Dinerman JL, Snyder SH (1994) Nitric oxide: a physiologic messenger. *Ann Intern Med* 120(3): 353-356.

- 227-237.
42. Lupien SJ (2005) Hormetic Influence of Glucocorticoids on Human Memory. *Nonlinearity Biol Toxicol Med* 3(1): 23-56.
  43. Ma H, Lesné S, Kotilinek L (2007) Involvement of beta-site APP cleaving enzyme 1 (BACE1) in amyloid precursor protein-mediated enhancement of memory and activity-dependent synaptic plasticity. *Proc Natl Acad Sci USA* 104(19): 8167-8172.
  44. Mattson MP (1997) Cellular actions of beta-amyloid precursor protein and its soluble and fibrillogenic derivatives. *Physiol Rev* 77(4): 1081-1132.
  45. Mattson MP (2004) Pathways towards and away from Alzheimer's disease. *Nature* 430(7000): 631-639.
  46. Mattson MP (2008a) Glutamate and neurotrophic factors in neuronal plasticity and disease. *Ann N Y Acad Sci* 1144: 97-112.
  47. Mattson MP (2008b) Hormesis and disease resistance: activation of cellular stress response pathways. *Hum Exp Toxicol* 27(2): 155-162.
  48. Miller GA (1956) The magical number seven, plus or minus two: Some limits on our capacity for processing information. *Psychological Review* 63(2): 81-97.
  49. Morris RG, Anderson E, Lynch GS (1986) Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5. *Nature* 319(6056): 774-776.
  50. Nadel L, Samsonovich A, Ryan L (2000) Multiple trace theory of human memory: computational, neuroimaging, and neuropsychological results. *Hippocampus* 10(4): 352-368.
  51. Nitsch RM, Farber SA, Growdon JH (1993) Release of amyloid beta-protein precursor derivatives by electrical depolarization of rat hippocampal slices. *Proc Natl Acad Sci USA* 90(11): 5191-5193.
  52. O'Mara SM, Commins S, Anderson M (2000) Synaptic plasticity of the hippocampal area CA1-subiculum projection: implications for theories of memory. *Hippocampus* 10(4): 447-456.
  53. Oddo S, La Ferla FM (2006) The role of nicotinic acetylcholine receptors in Alzheimer's disease. *J Physiol (Paris)* 99(2-3): 172-179.
  54. Ondrejcek T, Klyubin I, Hu NW (2010) Alzheimer's disease amyloid  $\beta$ -protein and synaptic function. *Neuromol Med* 12(1): 13-26.
  55. Pan KM, Baldwin M, Nguyen J (1993) Conversion of  $\alpha$ -helices into  $\beta$ -sheets features in the formation of the scrapie prion proteins. *Proc Natl Acad Sci USA* 90(23): 10962-10966.
  56. Paxinos G (1998) Mouse brain in stereotaxic coordinates, Academic Press, New York.
  57. Plant LD, Boyl JP, Smith IF, Peers C, Pearson HA (2003) The production of amyloid- $\beta$  peptide is a critical requirement for the viability of central neurons. *J Neurosci* 23(13): 5531-5535.
  58. Podlisny MB, Walsh DM, Tseng BP, Rydel RE (2000) The oligomerization of amyloid beta-protein begins intracellularly in cells derived from human brain. *Biochemistry* 39(35): 10831-10839.
  59. Puzzo D, Vitolo O, Trinchese F (2005) Amyloid-beta peptide inhibits activation of the nitric oxide/cGMP/cAMP-responsive element-binding protein pathway during hippocampal synaptic plasticity. *J Neurosci* 25(29): 6887-6897.
  60. Puzzo D, Palmeri A, Arancio O (2006) Involvement of the nitric oxide pathway in synaptic dysfunction following amyloid elevation in Alzheimer's disease. *Rev Neurosci* 17(5): 497-523.
  61. Puzzo D, Privitera L, Fa' M, Staniszewski A (2011) Endogenous amyloid- $\beta$  is necessary for hippocampal synaptic plasticity and memory. *Ann Neurol* 69(5): 819-830.
  62. Puzzo D, Privitera L, Leznik E (2008) Picomolar amyloid-beta positively modulates synaptic plasticity and memory in hippocampus. *J Neurosci* 28(53): 14537-14545.
  63. Qiu WQ, Ferreira A, Miller C (1995) Cell-surface beta-amyloid precursor protein stimulates neurite outgrowth of hippocampal neurons in an isoform-dependent manner. *J Neurosci* 15(3): 2157-2167.
  64. Randall AD, Witton J, Booth C (2010) The functional neurophysiology of the amyloid precursor protein (APP) processing pathway. *Neuropharmacology* 59(4-5): 243-267.
  65. Renbaum P, Levy-Lahad E (1998) Monogenic determinants of familial Alzheimer's disease: presenilin-2 mutations. *Cell Mol Life Sci* 54(9): 910-919.
  66. Rezvani AH, Levin ED, Buccafusco JJ (2006) Involvement of the NMDA System in Learning and Memory, in: (Eds.),

Animal Models of Cognitive Impairment. CRC Press, Boca Raton (FL), chapter 4.

67. Berezovska O, Lleo A, Herl LD (2005) Familial Alzheimer's disease presenilin 1 mutations cause alterations in the conformation of presenilin and interactions with amyloid precursor protein. *J Neurosci* 25(11): 3009-3017.
68. Pesci G (2012) Teoria e Pratica della Psicomotricità Funzionale, Roma.
69. Pesci G (2009) La Psicomotricità Funzionale. Scienza e Metodologia, Roma.
70. Pesci G (2007) Metodologie, metodi e tecniche di rilassamento motorio muscolare, Edizioni Scientifiche ISFAR, Firenze.
71. Pesci S (2011) Abilitazione-Riabilitazione, Edizioni Scientifiche ISFAR, Firenze.
72. Pesci G, Bulli L, Ricci P (2005) Bilancio Psicomotorio Funzionale, Edizioni Scientifiche ISFAR, Firenze.
73. Pesci G, Zoccolini L (2014) Linguaggio verbale e fonemico nel principio sistemico, Edizioni Scientifiche ISFAR, Firenze.
74. Pesci G, Ricci P (2014) Psicocontatto, Edizioni Scientifiche ISFAR, Firenze.
75. Zigmond MJ, Bloom FE, Landis SC (2002) Neuroscienze. Edises, Naples.

## Bibliografia

1. Maggini S, Pierre A, Calder PC (2018) Immune Function and Micronutrient Requirements Change over the Life Course. *Nutrients* 10(10): 1531.
2. Prietl B, Treiber G, Pieber TR, Amrein K (2013) Vitamin D and Immune Function. *Nutrients* 5(7): 2502-2521.
3. Rodrigues C, Percival SS (2019) Immunomodulatory Effects of Glutathione, Garlic Derivatives, and Hydrogen Sulfide. *Nutrients* 11(2): 295.
4. Tilg H, Moschen A R (2015) Food, Immunity, and the Microbiome. *Gastroenterology* 148(6): Pg No. 1107-1119.
5. Brown G D (2011) Innate antifungal immunity: the key role of phagocytes. *Annual Review of Immunology* 29: 1-21.
6. Meijerink M (2018) Structure dependent-immunomodulation by sugar beet arabinans via a SYK tyrosine kinase-dependent signalling pathway. *Frontiers in Immunology* 9: 1972.
7. Lamas B, Natividad JM, Sokol H (2018) Aryl hydrocarbon receptor and intestinal immunity. *Mucosal Immunology* 11: 1024-1038.
8. Jonna Koper (2020) The gut way to health: in vitro studies on immunomodulatory food compounds.
9. Gutiérrez-Vázquez C & Quintana F J (2018) Regulation of the immune response by the aryl hydrocarbon receptor. *Immunity* 48(1): 19-33.
10. Laura Giusti, Cristina Angeloni, Silvana Hrelia (2018) A Proteomic Approach to Uncover Neuroprotective Mechanisms of Oleocanthal against Oxidative Stress. *Int J Mol Sci* 19(8): 23-29
11. Ghosh TS, Rampelli S, Jeffery IB (2020) Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries. *Gut* 69(7).