Mind Switches: Everything That Needs to Change to Favour Change

How to work on the 4 key elements at the heart of change: neuroplasticity and metabolism, system balance, brain networks and hubs, natural flows

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FEATURE

LEVELS OF CHANGE

What needs to change to favour change?

Philosophy first and psychology later have been posing this very question for a long time. The answers, depending on the authors and their different outlooks, are various: examples include acquired patterns, influences, internal representations, mindsets, automatisms, and more.

Over the years, research and clinical experience have confirmed that all these are equally valid models of interpretation, although each is different (Kamenov, Twomey, Cabello, Prina, & Ayuso-Mateos, 2017). It is useful, therefore, to consider what connects these processes, what other factors affect change, and which are effective (Bandelow et al., 2017). A scientific and pragmatic approach consists of shifting the level of analysis by examining the problem from a different perspective so that our question becomes: what changes when we modify acquired systems, influences, representations, memories, and so on?

A first answer can be found at the structural level—that is, change in the synaptic connections activated by a specific stimulus. A real-life example of this could be when a person sees a spider, which activates a fear response, and a neural pathway of a–b–c–d neurons activate in sequence. After effective therapy, however, the pathway may change, and a–b–f–z neurons (say) activate instead. This change is dependent on neural plasticity that enables new neu-

ral pathways and connections to develop. This process can be nurtured with some practical strategies and tools as provided by the therapist during the psychotherapy process to improve its effectiveness.

A second answer relates to the system level—by which we mean the balance of different systems in the body. When we say "further to trauma the amygdala remains hyperactive and triggers unnecessary anxiety responses", what has changed? From a functional–anatomical perspective, a hyperactive amygdala is an inflamed amygdala, in the same way that excessive physical exertion can cause a swollen knee that hurts at the slightest touch. Understanding these different processes allows us to act synergistically on more than one level at the same time. In psychotherapy, and indeed in any change process, it is possible to reduce the inflammation and normalise the amygdala's response, occasioning less intense defensive responses and making room for mentalization through targeted exercises and instruction—just as an anti-inflammatory drug provides relief to a swollen knee and enables initial rehabilitation movements.

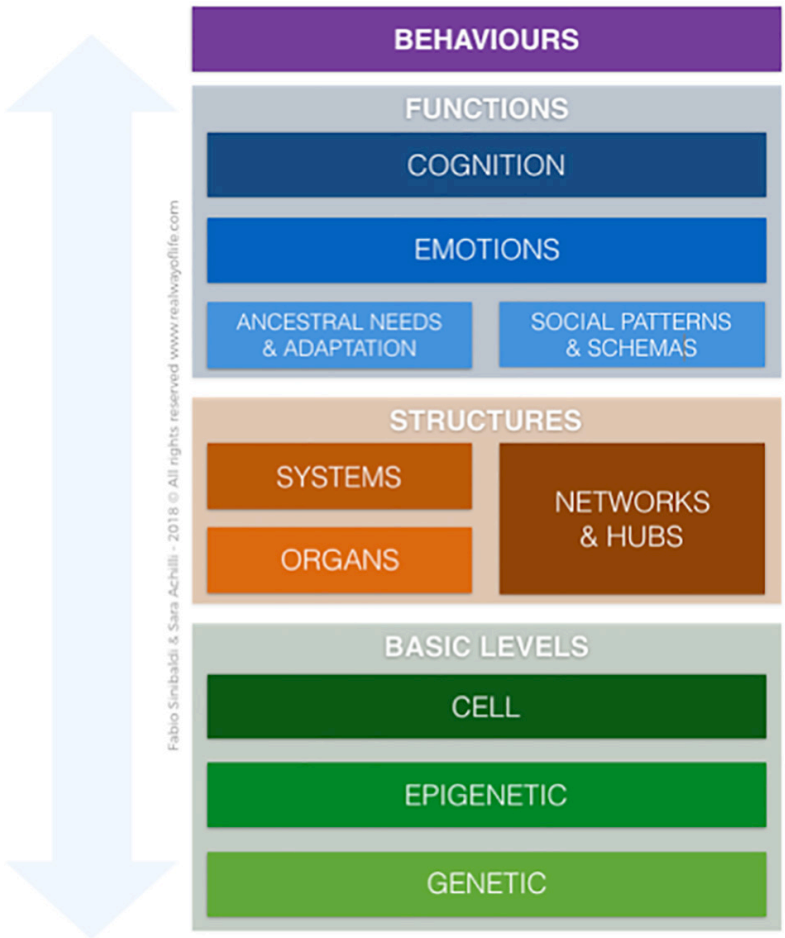

Figure 1. Breakdown of all connected levels with heterarchical links (nonlinear hierarchies) at the core of any mind–body process.

CHANGE SWITCHES

These two examples illustrate the idea of *change switches*, or the steps to be taken from a dysfunctional state—featuring little neural plasticity, inflammation, misuse of cellular energy, failure to use interoceptive data, and many other phenomena that feed the problem (such as inflexible opinions, inability to read contextual clues correctly, low modulation of emotional responses, etc.)—to a functional state that instead favours the recovery of a

physiological condition during adaptation and change processes.

Change switches are metaphorical switches that need to be "flicked" to promote flexible and evolutionary adaptation processes. These systems do not operate according to an on/off dichotomy but follow a series of gradual steps that can be worked on in a targeted way. The switch metaphor actually highlights the need to change the state in order to activate the required change. In visual terms: to switch on a light bulb, you need to flick the switch up or down so as to drive electricity to it, but if the electricity doesn't flow or is intermittent, it will be difficult to do anything in that room (such as reading or working) in an ongoing and satisfying way.

We've classified the different switches according to two criteria. The first relies on reverse engineering by identifying what changes have occurred in people who have achieved a lasting and effective change. The other method is through a process of summarisation and integration, where we look at different disciplines for the most efficient elements and processes that promote change to well-being and physiological states, such as EMDR (eye movement desensitization and reprocessing), mindfulness, meditation, verbal and physical psychotherapy, structured training and coaching techniques, and others.

In this enterprise we have been supported by a network of global professionals linked to the Integrative Sciences Hub (https://www.realwayoflife.com/en/hub/) who contributed data from clinical practice and took part in forums and research groups both online and in person. The primary focus of our work has always been a split between clinical evidence and ease of application in professional practice.

Here we provide an in-depth analysis of the four categories we've designated to the different switches, defining each category by type and degree of functional interaction. First-level switches provide the foundation for the following levels, but all levels can provide significant retro-feedback on the previous levels.

The four major groups of switches are:

1. Neural plasticity, energy and epigenetics;
2. The science of psychosomatics: system balance;
3. Networks and hubs: emotions and behaviour management headquarters; and
4. Natural flows: doing your best, fluidly.

In addition, there is a practical operating system to manage all these aspects (outlined below), as well as tips, techniques and strategies to introduce them into your own professional practice.

1. Neural plasticity, energy and epigenetics

This level provides answers to the questions—

- Where and how are new ways of thinking, effective emotional responses, and all new skills developed?
- Where can we draw the greatest energy and vitality?

These are the basic cell-level switches. The cell represents the basis of life and carries out all the essential functions that we need to enable change: neural plasticity (connecting and exchanging messages with other cells), energy metabolism (providing us with the energy to tackle any type of adaptation or development) and changing gene expression (through epigenetic markings which are at the heart of long-lasting changes).

The three levels of neural plasticity and energy availability

As described in the introductory paragraphs, from a neurobiological point of view, any change or learning corresponds to changes in neural networks. The pathways previously traced by neurons are abandoned, and new ones that are more effective and support new behaviours are created.

We sometimes hear talk of boosting and supporting neural plasticity, or of developing new connections, or even of developing integration (both inter-hemispherical and other types), and again we need to ask: what does this mean in practical terms and how can it be achieved?

It's important to note that there are different levels of plasticity. Each level, listed below, is equally important and useful in providing the opportunity for change and greater flexibility in adaptation processes:

1. intracellular (with numerous mitochondria),
2. intercellular (between neurons), and
3. extracellular (ECM).

The intracellular level concerns the number of mitochondria in each cell. Mitochondria represent the power house of the cell and have a key role in managing the development of new neural networks and eliminating connections that are no longer in use. The bioenergetic metabolism of the mitochondria also influences epigenetic marking processes that, in turn, enable lasting changes in the regulation of physiological processes linked to the expression of emotions and various mental and psychosomatic processes (Mattson, Moehl, Ghena, Schmaedick, & Cheng, 2018). The more mitochondria present in a neuron means the more available they are to help it perform its role of signalling and providing energy for its cognitive–emotional duties.

The intercellular level is the most well-known and refers to the development of new neural networks. These are the structures at the basis of brain networks (which we will analyse in groups 2 and 3) that respond in a significant way to sensory stimuli, motor outputs, and environmental stimulation. In the world of professional practice this means that it is possible to favour plasticity via nutritional advice and a range of stimuli and multi-sensory activities, introducing and integrating therapy or development processes with highly experiential activities posing an appropriate level of adaptation challenge (Stranahan et al., 2009; Yuste & Bonhoeffer, 2001).

When neural integration between hemispheres, or even between different brains (cf. MacLean, 1990) is discussed, it is not just connections between neurons but also the connecting structures that nourish and support them that are considered. In fact, the third

level of plasticity relates to the extracellular matrix (ECM), which changes depending on the stimuli it receives, allowing the neural and astrocyte (glial cells) cytoskeletons to combine to exchange organelles and other substances (Damasio, 2013).

The ECM is stimulated by direct physical contact such as massage and manual techniques, and also by indirect movement such as stretching, sport, and psycho-physical techniques.

Energy, efficiency and physiology

There are other important switches at cellular level that regulate energy and the physiology of change and well-being.

Let's look at a practical example—anxiety, say—which has certain typical symptoms such as: feeling disoriented, feeling faint, lack of motor control, loss of long-term objectives, among others.

Now, let's ask ourselves once more what sustains these processes at a basic neurological level.

The first conceptual revolution relates to the metabolism of neurons, in particular their mitochondria. Contrary to popular belief, only 10% of the work of mitochondria is based on glycogen derived from sugars (Fontán-Lozano et al., 2008), while they use quality fats that they transforms into ketones far more effectively. The latter represent the most efficient source of energy for our nervous system cells (Maalouf, Rho, & Mattson, 2009; Marosi et al., 2016), providing them with constant energy to carry out their tasks in support of their duties of alert, control and resolution of external threats.

Feeling disoriented, a fuzzy head, and shaking limbs (hands trembling and legs giving way) are all symptoms that relate to a lack of oxygen to the brain and muscles (Radak, Zhao, Koltai, Ohno, & Atalay, 2013). These need to work effectively to activate the fight-or-flight responses required in dangerous conditions. Oxygen is, in fact, the second key element relating to these switches.

It is not by chance that controlled breathing techniques play a key part in helping people recover from early-stage anxiety and panic attacks. However, once oxygen arrives to a cell it still needs to be put to use. Mitochondria (they are the users of oxygen) must therefore be in a responsive physiological state and, if they are numerous, they will be able to take up oxygen more rapidly (see above). By these means, it is thus possible to gain greater control, more quickly, of basic self-regulation processes with their connected history of mastery and personal efficiency in stressful circumstances.

2. The science of psychosomatics: System balance

The questions this level responds to—

- In what instances and how does stress turn into disease?
- What physical changes can alter the workings of the mind, emotions and behaviour?

This section takes us up a notch in the complexity stakes and we will see which switches need to be activated at system level. In this

case, too, we are dealing with complex and multifaceted systems, but we can roughly divide them into two major categories:

1. the relationship between immune system inflammation and emotional, cognitive and neurodegenerative dysfunctions;
2. allostatic load, or in other words, the price to pay in conditions of over-adaptation and chronic stress.

Worried mind–inflamed brain–inflamed body

Any patient who is diagnosed with any of the different forms of anxiety, stress, depression or post-traumatic stress disorder (PTSD) also presents an inflamed immune system akin to that of patients being treated for common bacterial or viral infections or for strictly physical trauma (Michopoulos, Powers, Gillespie, Ressler, & Jovanovic, 2017). This inflammation coincides with the processes known to follow traumatic events and chronic stress such as the hyperactivation of certain areas of the brain (e.g., the amygdala, which increases fear responses and symptoms of anxiety) and the dysfunction and reduction of other areas (e.g., the hippocampus, which under these conditions causes a loss of sense of direction and memory, etc.).

An important discovery has been made in this area from a clinical perspective: the association of a basic anti-inflammatory drug such as aspirin with an anti-depressant, or with cognitive-behavioural psychotherapy, increases the remission of depression in patients previously unresponsive to exclusively pharmaceutical or psychotherapeutic therapies (Mendlewicz et al., 2006). In other words, inflammation represents one of the possible causes of resistance to change. This discovery completely revolutionises traditional approaches towards resistance to change as being due to purely psychological or biological factors.

From a practical point of view it is important to highlight that there are more anti-inflammatory solutions that are particularly effective than simply pharmaceuticals—such as improved nutritional habits, aerobic exercise, relaxation techniques and other structured activities.

Stressed to the limit—where flexibility ends and takes its toll

The allostatic load concept introduced by Bud Craig (2002, 2015) and now widely acknowledged and developed by the scientific community represents the other side of the adaptation coin.

Allostasis is the adaptation process through which we try to reach stability or homeostasis via behavioural or physiological changes.

When disadvantages are greater than advantages and the condition extends excessively over time, we pay a price both in structural (damage to organs, excess of neurotoxins, resistance to neurotransmitters, etc.) and functional (inability to tolerate further stress, drop in motivation, maintaining recovery or flight postures, etc.) terms (Juster, McEwen, & Lupien, 2010).

Monitoring and actively managing the switch between increasing the level to gain advantages and establishing rest and recovery processes to go back to the physiological state

is a key strategy in maintaining the processes without paying a toll for it.

In fact, our tendency to get used to things, to put up with discomfort, effort and pain, if prolonged, is linked to a decrease in grey-matter volume, changes to cortex width (Baliki, Baria, & Apkarian 2011), or even alterations to the organisation of the networks that manage pain and interoceptive circuits, which are critical to self-regulation, elaborating emotion, and developing identity and social awareness (Maleki & Gollub, 2016).

3. Networks and hubs: Emotion and behaviour management headquarters

The questions this level responds to—

- What are the different stages—at every level—that can lead a person to activate a stress response, to feel fear, or activate an aggressive response?
- What triggers a defence mechanism rather than the ability to carry out objectives to completion?

Previously, the neuroscience of emotions and behaviour has focused on two extremes: the study of brain areas (i.e., the amygdala as the "fear hub") or large multi-function systems (i.e., the limbic system as the "manager of emotions and social interaction"). Over time research has progressed and a configuration of networks and hubs has emerged (Pessoa, 2013)—that is, a grouping of areas that, in dynamic interaction with each other, carry out the functions of emotional regulation, cognition, problem solving, social rules, and so on.

Different networks are related to specific functions. We will now analyse two of the main systems at the core of self-regulation. These are interesting switches to focus on and act in a structured way on adaptation, development or recovery processes, alternating them so that they can sustain and feed each other.

The danger-and-resource-analysing switch

The study of brain networks took a significant leap forward with the identification of three circuits that highlight what happens in our brain when we shift from a condition of quiet and introspection (the default-mode network) to one of alarm and evaluation of danger (the salience network, connected to conditions of anxiety, fear, stress, etc.) right through to putting into action resolution or adaptation (the executive network, which activates processes of fight, flight and self-regulation).

The salience network (SN) is, in effect, a switch in that it allows the activation of one system to another, between the default-mode network and the executive network (Brooks & Stein, 2015).

As the name suggests, the SN evaluates what is salient, or relevant. A sound, a shape, a change in temperature, a texture, are all signals that the SN evaluates to assess whether there is a need to adapt at a physiological or behavioural level—the SN thus represents the starting point of all emotional and defensive processes and behaviours relating to the adaptation to an environment. A condition of continuous alert, such as the anxiety caused by PTSD, can therefore be considered in this light as the prolonged and dysfunctional maintenance (no longer suited to the context) of SN

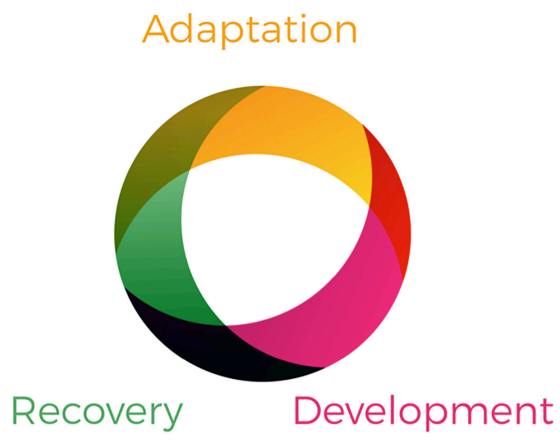

Figure 2. Graphic summary of the relationship between basic adaptation, recovery and development functions highlighting the significant areas of interaction and crossover between the three processes, which support each other and need to remain in dynamic balance to achieve optimal synergy and potential. Adapted from F. Sinibaldi and S. Achilli, 2018, *The Switch: A Guide for Professionals Driving Change Effectively on Every Level. Transformative Mindfulness: 45 Exercises*. Copyright by Real Way of Life.

activity. We need to ask what keeps it in this state and which of its functions is not finding a response that enables it to deactivate—that is, to recognise termination signals (Sinibaldi & Achilli, 2018) or to engage another functional network. Too often the evaluation of danger places too much emphasis on external factors and their evaluation. The study of the SN, instead, highlights how these considerations also depend largely on the insula, which gives much importance to information such as body maps, muscle readiness and muscular power, freedom of movement and, in synergy with the periaqueductal grey, the potential physical damage that can be caused or suffered. Techniques and psychophysical exercises that integrate these data will make the process of therapy more targeted and effective in recovering the basic functions of self-regulation (Sinibaldi, 2018).

The switch that analyses the environment and personal objectives

A transversal concept that can be applied in an integrated way with different approaches relating to the management of stress and anxiety is that of uncertainty, or the idea of unpredictability that also carries with it feelings of hostile environments and lack of safety.

Uncertainty is a broad concept that covers various different aspects of daily life such as parental behaviour or that of your partner, work security, lack of social support, or features of the external environment.

While looking for balance between adaptation and development, the brain receives sensory data from the internal and the external world (interoception) and selects a switch based on an evaluation of whether it is more useful: (a) to carry on trying to reach its objectives, (b) to act on the outside world altering it, or (c) to act on its own body, changing its physiology (i.e., the stress response).

In this instance the switch relates to two main processes and is based on the evaluation of three different elements regulated by specific networks and hubs (Peters, McEwen, & Friston, 2017), namely:

1. information regarding the state of things within and without the body;
2. information relating to the predicted

state as realistically expected and attainable; and

3. information relating to ideal objectives.

The anterior cingulate cortex interacts with these representations, which the neural hubs elaborate, comparing attainable state with objectives. On the basis of this evaluation, it selects the best strategy for its future well-being.

If there are conditions of certainty, then the pre-supplementary motor area and the primary motor cortex start their specific behavioural responses. If, instead, the conditions are unpredictable (i.e., low predictability of the environment or high uncertainty in the choice of an optimal strategy), the amygdala activates a stress response.

In this latter instance, significant alterations are activated that in the short term can literally save our lives and bring advantages, but that in the long term can degenerate into a condition of supercharged allostasis and consequent malfunctioning of the adaptation mechanisms themselves (causing anxiety, panic attacks or depression) and systemic degeneration of the organs involved (heart attack, chronic exhaustion, gastritis, IBS, nervous system tissue diseases, postural and motor dysfunctions, etc.).

Restoring the appropriate switch process between the achievement of goals and stress responses, therefore, becomes essential. To do this, it is necessary to act on elements that generate the greatest response among those involved in this network—such as the appropriate perception and evaluation of unpredictable elements or the alternation of physical and mental environments by presenting different degrees of hostility throughout the day (e.g., with a parachute or exit systems and numerous other processes).

4. Natural flows: Doing your best, fluidly

Questions this level responds to—

- How can direct action on thought and behaviour be most effective?
- Can you change how you think and behave naturally?

This level is concerned with final-stage switches for the processes described so far. It looks at how to act on behavioural, creative, postural, motor, interpersonal, and communication flows that are activated in order to adapt to an environment, develop something new (e.g., an ability or potential relationship), or recover energy and maintain a condition of balance.

One key point that relates to all flows is that of the feeling of naturalness and spontaneity. People often refer to their way of speaking, deciding or acting spontaneously but at the same time they do not perceive it to be entirely free and feel the urge to improve this. Let's look at some examples that highlight how often this feeling emerges from the awareness (maybe only just hinted at) that complete freedom and flexibility of execution are not present. By contrast, recovering the physiological state of these flows and the processes that compose them allows us to support more natural ways of being, a feeling of mastery, and to perform biofeedback that favours the physiological state of the previous level switches.

Self-assessment and improvement

Our first example focuses on a specific instance of creative flow. These flows relate to the development of new ideas, also the acceptance of new points of view and integration of new information, using these processes to favour creative or problem-solving activities.

When the creative flow is directed inwards—toward our own ways of thinking and behaviours—we talk about metacognitive ability or the ability to accurately judge our own performance (e.g., any communicative, interpersonal action or decision). There are specific networks and systems that, if functioning appropriately, can have a significant impact on metacognitive abilities and access to different levels of awareness that effect self-confidence and feelings of mastery, elements that are critical to the feeling that something is natural and to any action that balances spontaneity and control.

Various studies have shown the areas that support metacognitive management in the frontal and parietal lobes (Fleming & Dolan, 2012) and have identified the features that make it a capability that can be exercised in a structured way.

It is therefore possible to develop an initial and basic ability to change: the ability to self-observe and appropriately identify the aspects that need to improve to make a switch from poor metacognition, which is not self-responsible, to a flexible and evolutionary mode. One of the most effective ways relates to the use of direct, immediate feedback in real-life circumstances (Carpenter et al., in press). Thanks to technology, this process is easy to put into action nowadays (and much appreciated by end users, as we can see in our research lab and clinical practice every day), whereby the therapist, trainer or instructor can see or hear the patient in action from a distance and provide feedback and suggestions for alternative strategies in action.

Freedom of movement = emotional and mental freedom

There are some interesting connections between muscular activation and emotional responses. In particular, there are a series of connections and interactions between stress responses and certain movements or postures that are taken to adapt to an environment, or in response to danger. For example, if a person who is in a good or neutral mood thinks about something negative, even for an instant, that immediately weakens the strength of isometric contractions (when muscle length doesn't change, such as when pushing your arms against a wall or remaining immobile), while there is no effect on an isotonic push (e.g., doing push ups), in free movement, or in flexible postures (Hillman, Rosengren, & Smith, 2004). This understanding has helped us develop specific techniques that alternate isometric contractions and muscle lengthening, in coordination with mental states and contextual clues, so as to bring muscle tone back to its physiological state (i.e., hypo- or hyper-active in conditions of chronic stress, or further to trauma) and to the appropriate state of activation or deactivation depending on requirements (Sinibaldi & Achilli, 2017, 2018).

The employment of high-concentration and intentionally slow micromovements (Schleip 2003) enables the development of an awareness

of our own unconscious adaptation systems in interpersonal dynamics—tensing of the neck, for example, or a shifting of the centre of gravity when we perceive a challenge or feel subject to social exclusion. The targeted use of these micromovements, in combination with a therapist or instructor who can suggest different types of interactions, allows the patient to develop both greater awareness and mastery over these processes. This strengthens the ability to focus and sharpens self-control in stressful inter-personal relationships by learning how to actively manage these forms of interpersonal adaptation.

There are other types of flows that cover all levels of behaviour: creative, logical, mindset, perception systems, interrelation abilities, motivation, posture and movement, physical condition, energy condition, and many more.

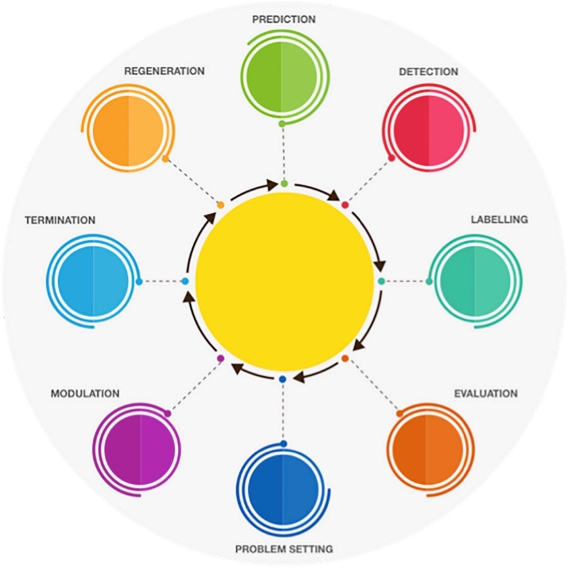

Figure 3. A summary of all the phases and processes involved in adaptation (stress, emotions, etc.) and development responses (learning, exploring, creation, etc.). Adapted from F. Sinibaldi and S. Achilli, 2018, *The switch: A guide for professionals driving change effectively on every level. Transformative Mindfulness: 45 exercises*. Copyright by Real Way of Life.

We cannot analyse each one in this article, but the idea is that in every instance we identify the neurobiological processes according to which change on each level represents a lasting switch, providing retro-feedback and supporting change on all other structural, metabolic, and functional adaptations taking place.

CONCLUSION: AN INCLUSIVE AND PRAGMATIC METHOD TO MANAGE COMPLEXITY

We have touched upon various issues and aspects of practical application concerning large and complex systems, for which there is much more to describe. We trust, nevertheless, to have provided a suitable grounding and some practical tips on how—through an integrated, integrative, and multi-dimensional approach—actions can be taken on various levels to favour change and well-being.

As there are many elements that interact with one another, and given the importance of respecting the appropriate sequence of activity, over time we have developed an integrative system that allows you to manage all the switches and to introduce them into therapeutic or training work. These are the integrative functional patterns. As the name suggests, they were developed to manage in a progressive and localised way all the elements at play (the neural networks involved, the role of prediction, expectations, objectives, trust, the delicate balance between adaptation processes and emotional memories, interpersonal relations, environmental elements, nutritional elements, and other aspects) with a significant focus on hu-

man behaviour in the widest sense of the term.

Integrative functional patterns enable the following of a logical and structured programme, acting on pre-existing conditions (e.g., metabolic states, inflammation, first- and second-level switches) that alter the early perception stages of an internal or external stimulus followed by appropriate evaluation (a multi-phase process including pre-logical and sensory phases as well as more structured and complex phases and the third-level switches), including the deepest motivational elements in common to all mammals that cause psychosomatic damage in case of deprivation (ancestral needs). The later stages include elements of self-monitoring (metacognition), planning and strategy, right through to physical and behavioural execution (flows from the fourth group of switches). The final phases are those of termination and regeneration, where it is possible to end the adaptation process and return the system to a healthy physiological state and prevent conditions becoming chronic by hyperarousal, traumatic memories, or other dysfunctional elements being carried through from the adaptation process.

In this heterarchical and circular perspective (non-linear hierarchies) on the adaptation-development-recovery process, each phase enables action that reinforces the abilities and capabilities that are a prerequisite, or are fundamental to the functioning of the subsequent phases, such as the feeling of mastery and control, mental and physical flexibility, and an increased degree of freedom of movement, but also of behavioural choice and greater energy for movement and action initiation and to sustain motivational and creative impulses.

REFERENCES

Baliki, M. N., Baria, A. T., & Apkarian, A. V. (2011). The cortical rhythms of chronic back pain. *The Journal of Neuroscience, 31*(39), 13981–13990. doi:10.1523/JNEUROSCI.1984-11.2011

Bandelow, B., Baldwin, D., Abelli, M., Bolea-Alamanac, B., Bourin, M., Chamberlain, S. R., . . . Riederer, P. (2017). Biological markers for anxiety disorders, OCD and PTSD: A consensus statement. Part II: Neurochemistry, neurophysiology and neurocognition. *The World Journal of Biological Psychiatry, 18*, 162–214. doi:10.1080/15622975.2016.1190867

Brooks, S. J., & Stein, D. J. (2015). A systematic review of the neural bases of psychotherapy for anxiety and related disorders. *Dialogues in Clinical Neuroscience, 17*, 261–279.

Carpenter, J., Sherman, M. T., Kievit, R. T., Seth, A., Hakwan, L., & Fleming S. (in press). Domain-general enhancements of metacognitive ability through adaptive training. *Journal of Experimental Psychology*. Retrieved from https://www.biorxiv.org/content/biorxiv/early/2018/08/10/388058.full.pdf

Craig, A. D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature Reviews: Neuroscience,* 3, 655–666. doi:10.1038/nrn894

Craig, A. D. (2015). *How do you feel? An interoceptive moment with your neurobiological self.* Princeton, NJ: Princeton University Press.

Damasio, A., & Carvalho, G. B. (2013). The nature of feelings: Evolutionary and neurobiological origins. *Nature Reviews: Neuroscience, 14*, 143–152. doi:10.1038/nrn3403

Fleming, S. M., & Dolan, R. J. (2012). The neural basis of metacognitive ability. *Philosophical Transactions of the Royal Society B: Biological Sciences, 367*(1594), 1338–1349. doi:10.1098/rstb.2011.0417

Fontán-Lozano, A., Sáez-Cassanelli, J. L., Inda, M. C., de los Santos-Arteaga, M., Sierra-Domínguez, S. A., . . . Carrión, A. M. (2008). Caloric restriction increases learning consolidation and facilitates synaptic plasticity through mechanisms dependent on NR2B subunits of the NMDA receptor. *The Journal of Neuroscience, 27*(38), 10185–95. doi:10.1523/JNEUROSCI.2757-07.2007

Hillman, C. H., Rosengren, K. S., & Smith, D. P. (2004). Emotion and motivated behavior: Postural adjustments to affective picture viewing. *Biological Psychology, 66*, 51–62. doi:10.1016/j.biopsycho.2003.07.005

Juster, R. P., McEwen, B. S., & Lupien, S. J. (2010). Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neuroscience and Biobehavioral Reviews, 35*, 2–16. doi:10.1016/j.neubiorev.2009.10.002

Kamenov, K., Twomey, C., Cabello, M., Prina, A. M., & Ayuso-Mateos, J. L. (2017). The efficacy of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in depression: A meta-analysis. *Psychological Medicine, 47*, 414–425. doi:10.1017/S0033291716002774

Maalouf, M., Rho, J. M., & Mattson, M. P. (2009). The neuroprotective properties of calorie restriction, the ketogenic diet, and ketone bodies. *Brain Research Reviews, 59*, 293–315. doi:10.1016/j.brainresrev.2008.09.002

MacLean, P. D. (1990). *The triune brain in evolution: Role in paleocerebral functions.* New York, NY: Plenum Press.

Maleki, N., & Gollub, R. L. (2016). What have we learned from brain functional connectivity studies in migraine headache? *Headache, 56*, 453–461. doi:10.1111/head.12756

Marosi, K., Kim, S. W., Moehl, K., Scheibye-Knudsen, M., Cheng, A., Cutler, R., . . . Mattson, M. P. (2016). 3-hydroxybutyrate regulates energy metabolism and induces BDNF expression in cerebral cortical neurons. *Journal of Neurochemistry, 139*, 769–781. doi:10.1111/jnc.13868

Mattson, M. P., Moehl, K., Ghena, N., Schmaedick, M., & Cheng, A. (2018). Intermittent metabolic switching, neuroplasticity and brain health. *Nature Reviews: Neuroscience, 19*, 63–80. doi:10.1038/nrn.2017.156

Mendlewicz, J., Kriwin, P., Oswald, P., Souery, D., Alboni, S., & Brunello, N. (2006). Shortened onset of action of antidepressants in major depression using acetylsalicylic acid augmentation: A pilot open-label study. *International Clinical Psychopharmacology, 21*, 227–231.

Michopoulos, V., Powers, A., Gillespie, C. F., Ressler, K. J., & Jovanovic, T. (2017). Inflammation in fear- and anxiety-based disorders: PTSD, GAD, and beyond. *Neuropsychopharmacology, 42*, 254–270. doi:10.1038/npp.2016.146

Pessoa, L. (2013). *The cognitive–emotional brain: From interactions to integration*. Cambridge, MA: The MIT Press.

Peters, A., McEwen, B. S., & Friston, K. (2017). Uncertainty and stress: Why it causes diseases and how it is mastered by the brain. *Progress in Neurobiology, 156*,164–188. 10.1016/j.pneurobio.2017.05.004

Radak, Z., Zhao, Z., Koltai, E., Ohno, H., & Atalay, M. (2013). Oxygen consumption and usage during physical exercise: The balance between oxidative stress and ROS-dependent adaptive signaling. *Antioxidants & Redox Signaling, 18*(10), 1208–1246. doi:10.1089/ars.2011.4498

Schleip, R. (2003). Fascial plasticity: A new neurobiological explanation: Part 1. *Journal of Bodywork and Movement Therapies, 7*, 11–19. doi:10.1016/S1360-8592(02)00067-0

Sinibaldi, F. (2018). Lavorare con l'unità corpo-mente per favorire pensieri, emozioni e sviluppo personale. In N. Barsotti, D. Lanaro, M. Chiera, & F. Bottaccioli (Eds.), *La pnei e le discipline corporee* (pp.). Milan, Italy: Edra-Elsevier.

Sinibaldi, F., & Achilli, S. (2016). *Transformative mindfulness: 45 exercises. An idea-a-day workbook to develop awareness and favour change*. London, United Kingdom: Real Way of Life.

Sinibaldi, F., & Achilli, S. (2017). *Handbook of integrative sciences: Evolution, adaptation, and physiology: Effective tools and techniques in a practical and modular approach to restore physical and mental health*. London, United Kingdom: Real Way of Life.

Sinibaldi, F., & Achilli, S. (2018). *The switch: A guide for professionals driving change effectively on every level.* London, United Kingdom: Real Way of Life.

Stranahan, A. M., Lee, K., Martin, B., Maudsley, S., Golden, E., Cutler, R. G., & Mattson, M. P. (2009). Voluntary exercise and caloric restriction enhance hippocampal dendritic spine density and BDNF levels in diabetic mice. *Hippocampus, 19*(10), 951–961. doi:10.1002/hipo.20577

Yuste, R., & Bonhoeffer, T. (2001). Morphological changes in dendritic spines associated with long-term synaptic plasticity. *Annual Review of Neuroscience*, 24, 1071–1089. doi:10.1146/annurev.neuro.24.1.1071