Studies in Philosophy of Science and Education
Homepage: https://scie-journal.com/index.php/SiPoSE
Email: sipose@scie-journal.com

p-ISSN: 2722-3523; e-ISSN: 2721-9267
SiPoSE, Vol. 6, No. 1, March 2025: 1-40
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Neurons and Glia Cells: Some Mention of their General Interrelationships

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Article Info

Article history:

Received February 3, 2025
Revised February 24, 2025
Accepted March 23, 2025
Available Online March 31, 2025

Keywords:

Glia cells;
Glia memory;
Super-will;
Voluntary thought;

ABSTRACT

In the present work we outline a hypothesis on what the role of glia cells could be in several operations processed by our brain. Going beyond the classical concept that attributes an almost ancillary function to glia at the service of neurons, and on the basis of what emerges from a lot of more or less recent studies about the possible glia-neuron collaboration in supporting many and diversified organic events, we intend to show how this functional synergy could be reasonably imagined as fundament of specific organic and mental processes both in the ordinary activity perspective and in the horizon of psycho-physical performances of higher level, where the exact meaning of psycho-physical performances of higher level will become later. In the frame of an evolutionary view of the human organism–considered in its wholeness–and of an evolution characterized by an increasing structural complexity, our aim is to present the idea (having to be carefully tested and developed in other contexts) according to which each organism is intimately driven to liberate itself from the contingency of the events occurring in the environment within which it is immersed. All this, in compliance with a general principle that seems to condition the living matter in its complex, that is, the principle of pursuing coenaesthesia, here generically conceived as the internal well-being which every organism wants to safeguard. The underlying persuasion is that evolution in complexity, tendency to a certain environmental emancipation and need for coenaesthesia, which the nature of living beings all together contains, can be better identified if we just begin to treat neurons and glia as a morphologic-functional unit that organically and systematically represents them.

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https://doi.org/10.46627/sipose

INTRODUCTION

A relatively recent but significant novelty in the broad and varied panorama of the so-called *neurosciences* is certainly represented by the interest reserved for the fundamental properties of the glial cells and their specific functions within the nervous system. Importantly, the early idea of glia, as cellular contribution having the mere task to support and protect the *nobler* neurons, has given way to the persuasion that such quantitatively preponderant component of CNS (central nervous system) and PNS (peripheral nervous system) might play crucially relevant roles in determining and modelling, in synergy with neurons, many organic processes once thought as governed exclusively by the latter. From this profound change in view, a plentiful flowering of different level and orientation studies have arisen, many of which of pioneering character and by facing this new mosaic of issues both with object-focused empirical investigations and with theoretical-conjectural purposes. The first type of approach, which can

be said *bottom-up* way, is undoubtedly the one that has generated most of knowledge on the morphological and metabolic properties of glial cells and on the strictly localized structural-functional relationships between such cells and neurons. After all, for the matter, it seems to be absolutely reasonable to address a topic, being still largely unknown, starting from basic questions such as those inherent to the intimate biological nature of the object taken into account. And this is how, thanks to rigorous, patient and detailed laboratory work, we have achieved the identification and fixation of some structural-functional-evolutionary specificities of glia which have become now cornerstones within research on the subject. Worth mentioning, for their relevance in shedding light on possible future investigation paths, are the notions *two ways neuron-glial communication*, *glial-glial communication*, *tripartite synapsis*, *glial plasticity* and *neuron-glial network functioning*. All concepts that have gradually consolidated just in experimental contexts.

Trailblazing works from a few decades ago (variously reviewed and amplified in the course of the years) revealed how perisynaptic astrocytes in CNS and terminal Schwann cells in PNS tend to develop intracellular Ca^{2+} concentration increases in response to the activation of neurons associated in an arrangement of synaptic proximity to the glial processes. This fact, highlighted especially by fluorescence microscopy, showed two crucial aspects: 1) these glial cells can be *activated*, although in a different way with respect to neurons and 2) the activation responds to the one of synapses in which they *participate* with their processes. But such discoveries represented a real trigger for the emergence of multiple issues to be studied. Questions immediately arising from those empirically encountered events were, for instance: how can this communication from neuronal synapses to glial cells occur? Is a reverse communication direction from glia to neurons also conceivable? What could be the functional value of such an exchange between structurally distinct cells being until then considered incapable of maintaining truly *intimate* relationships? Thus, based on similar theoretical problems, several experimental investigations have been conducted with the aim of clarifying the properties of what appeared to be a real neuron-glial dialogue construed according to some code with its own rules to formulate messages understandable to the participating cells.

Although a detailed report about the very vast range of researches carried out on this matter is over our present scope, it is anyway of interest here to recall the main scientific evidences acquired at the current state of art. Firstly, it has to be emphasized that the breakthrough offered by finding of varying intracellular Ca^{2+} concentrations (in terms of amplitude, frequency and duration) in response to synaptic activity was the turning point from which it turned out to be possible to identify a set of structural, chemical and metabolic features of glia (or some types of them) making such cells not only somehow similar to neurons in their reactive behaviour to stimulation but also functionally much closer to the latter than previously thought. In particular, it has resulted that glia are equipped with several neurotransmitters-binding receptors (such as glutamate, GABA, purines, monoamines and peptides receptors) that, once activated by their ligands and through specific second messengers, generate intracellular metabolic processes just leading to an increase of Ca^{2+} thus making these variations in Ca^{2+} concentration the hallmark of glial excitation (Volterra & Meldolesi, 2005). But that is not all. In parallel with the prerogative to be activated by neurotransmitters, glia have been found capable in turn of producing and exporting molecules identical to neurotransmitters or having neuroactive properties (then named also *gliotransmitters*), besides neurotrophic factors, and doing so in various ways, towards different targets and with supposedly specific final effects (Araque et al., 2002; Rose et al., 2003 and Zhang et al., 2003).

The increase in Ca^{2+} concentration, which spreads like a wave between contiguous glial cells by virtue of the gap-junction structure coupling them, induces the release of gliotransmitters according to the same chemical dynamics governing the release of neurotransmitters. However, the glial exportation of transmitters into the extracellular medium seems to be more articulated than the neuronal one. In fact, in addiction to vesicular exocytosis (which in glia is not limited to the area of synaptic clefts alone but possible along large stretches

of membrane) there are at least two other means of release: transmembrane channels and selective transporters. Beyond the precise mechanisms governing these export dynamics, which in truth are still little known in detail, it is important to observe that the ability of emitting substances with activating/modulating power on other cells both in a proximal and well-defined perspective (the area of shared synapses) and in a distal communication horizon – the extracellular medium *tout court* – is indicative of the existence of two neuron-glial interaction levels with presumably more distinct functional potentialities.

The proximal information exchange way (to date the better known of the two) is that exploited by perisynaptic astrocytes and terminal Schwann cells to act directly on the synapses covered through their processes and someway modulate the progress of transmission of the synapses themselves (Mauch et al., 2001; Song et al., 2002; Baldwin & Eroglu, 2017). The distal one is probably used to rule other forms of interaction with other emerging results. In any case, both are the proof of something difficult to reject: that is, the existence of a neuron-glial and glial-glial communication system whose architecture, although still largely unclear in its specificity, can be at least reduced to two basic level of expression. A first close dialogue level, involving the shared synapses – which now become precisely *tripartite synapses* – and in general neuronal and glial cells in close contact with each other, and a second level concerning the potential effectively possessed by glia to communicate with other glia and neurons even remotely from their physical locations. Until now, the first-level relationships have certainly been most studied – according to a bottom-up logic. The *microdomains*, i.e. the close relationship spaces between glia and neurons, have showed to possess a truly surprising set of properties that offer very interesting matter for future speculations. For instance, glia close to neurons, such as astrocytes in CNS, are not only tasked with clearing synaptic clefts and maintaining a chemically optimal environment for the related neurons, but they also show to have all the characteristics of an active participant in determining whether and how a certain information transmission has to be executed (Zonta et al., 2003). Some researches, mainly carried out on hippocampal regions and Bergmann glial cells in cerebellar Purkinje layer, have unequivocally confirmed the ability of perisynaptic astrocytes to modulate the synapses, shared by their processes, both by increasing the ongoing neuronal presynaptic action and inhibiting its force and to do this based on stimulation-dependent response ways that seem just to be governed by a well-precise encoding whose chemical-metabolic *grammar* has been only partially discovered (Perea & Araque, 2005; Matsui & Jahr, 2003; Matsui & Jahr, 2004; Perea & Araque, 2005. It is therefore clear how important is, in managing synaptic flows, to have suitable tools, such as external transporters, by which to work thoroughly to favour degradation and/or reuptake of transmitters or, vice versa, in turn providing additional activating substances depending on what appears to be necessary.

The microdomains are like microenvironments in which glia intervene by targeted actions and using, so to speak, highly precise surgical means. This, more generally, also applies to another basic typically glial task: i.e. the immune protection of neurons. In fact, as is well-known, some glia have been evolutionarily developed to function as safeguard against antigens or injuries of various types, thus carrying out the same task that the immune system carries out in the organism outside the nervous system (Brennemann et al., 2000; Marella & Chabry, 2004; Bate et al., 2005). Now, without going into detail, it is sufficient here to underline the crucial importance of glia both in maintaining and undermining the health and integrity of the nervous system in its whole and hence to reiterate the absolute essentiality of knowing better and better every type of information exchange that, within the microdomains as well as at the global level, can have some metabolic relevance in the overall homeostasis of the system. Such observations obviously hold beyond any issues strictly tied to the dynamics of tripartite synapses. Anyhow, as said above, glia (especially astrocytes) demonstrate to have reaction to excitation properties such as to suggest the existence of a much broader glial communication perspective than that one focused on synaptic relationships. Vesicular exocytosis spread along the cell membrane and release of glia-neuroactive substances into the extracellular medium, on the one hand, and

distal propagation of Ca^{2+} waves thanks to the gap-junction connection, on the other hand, make astrocytes presumably capable of diffusing chemical messages far beyond the narrow radius of a synapse. Indeed, it is not improper to speak of a *ubiquitous transmission of signals* by glia to contrast the latter with the more rigid one of the synaptic wiring to which neurons are subjected. Yet, what does it exactly involve? First of all, and trivially, it suggests that a more accurate identification of the biological dynamics supporting this wide-ranging communication would be at least desirable, also because to date very little is known about its properties and functioning. However, beyond this basic interest in the question, such a broadening of the horizon within the intimate nature of the nervous system, viewed as also including glia cells, opens up the possibility of formulating reasonable heuristic hypotheses of various kinds and with different theoretical contents. In other words, moving from a bottom-up vision to a top (down one) returning to the distinction between opposite research approaches introduced at the beginning, it might make sense, for example, to ask whether the biological framework of a communication potential broadened in this way could help to better seek and delineate the organic foundations from which certain faculties of fine and complex openness towards the environment, typically but not exclusively belonging to humans, originate. Anyhow, to do it, i.e. to attempt of defining some hypothesis on the neuron-glial origin of psycho-physical manifestations such as *will* or *thought*, with their structural allies such as *memory* and *emotion*, is necessary to adopt a way of seeing the matter different from that one of a bottom-up investigation.

Specifically, evidences showing a wide-ranging and somehow ubiquitous communication potential authorize to conjecture that such biological capacity could effectively contribute to forming the organic basis for the emergence of properties as concretely powerful as they are intimately enigmatic such as, precisely, thinking (meant *lato sensu*) or being able to make decisions of some kind on what is ahead. However, the reasonableness of hypotheses like this finds support just looking at the issue from a systemic point of view. This is to say that, if we want to treat a thought process or a voluntary action (i.e. a voluntarily decided action) as something that physically has its foundations in an expanded communication network involving all the main components of CNS, then it turns out to be clear that it is possible to approach matter in the right way only by dealing with the "protagonists of the story" (neurons and glia together) in a shared-network-functioning perspective. In this respect, it has to be noted that, for some time now, neurons have been also regarded at a level of communication networks and systems, as this has seemed to be the most suitable way to reach good results in understanding the organic origins of complex phenomena, among which psychic phenomena i.e. conditions having reverberations in terms of *first-person experience*. It is therefore here a question of extending such general approach even to glia and trying to imagine joint communication networks based on neuron-glial ensembles that work in local synergy and in a systemic horizon to allow high-biopsychic-impact events to emerge in their phenomenal proposition. Some recent findings about the *wide-ranging functional* properties of glia are certainly a promising framework within which to outline hypotheses on the structural foundations of organic faculties that expresses the results of their inner processes on the psychic plane (Delgado & Navarrete, 2023; Hirrlinger & Nimmerjahn, 2022; Becker *et al.*, 2022; Gordleeva *et al.*, 2021; Curreli *et al.*, 2022). And it appears even more sensible if we consider that such findings have, among other things, revealed a communication capacity of glia which, in some terms, equals the neuronal one and, in others, even surpasses it.

So, to conclude this introductory overview: in compliance with the following two cornerstones:

I) Concept of expanded communication within the neuron-glial complex and;
II) Seeing of neuron-glial dynamics as structured in cellular strictly related ensembles jointly functioning, at a first level, and as organized in more articulated processing networks aiming at a common goal, at a second level,

https://doi.org/10.46627/sipose.v6i1.409

our purpose is to define a general hypothesis on the possible neuron-glial functional mechanisms that allow the arising of higher psycho-organic faculties such as will, voluntarily determined thought and voluntary control of the primary and/or acquired emotional reactivity towards environmental and social stimulations. All this, following the idea that the neuron-glial system itself has evolved just responding to the basic need of the organism of which it is part to manage the vital relationship of the latter with the environment in an increasingly efficient and dominant way (Klämbt, 2013; Rossi, 2020).

RESULTS AND DISCUSSION

Coenaesthesis and Evolution in the Organic Structures

To provide a general background to our theoretical proposal, we report two concepts on which any view having the *life* as its own focus of interest is based.

I) Each living organism, in order to preserve itself, tends to reaching and keeping its inner *well-being* or, as it is also named, *coenaesthesia*.

Now, each organism (that unicellular too), for surviving within its own environment, has to possess the ability to respond to the stimuli coming from the latter. This, both to defend itself from external dangers and to seek what is necessary for its material subsistence. Such dual need can be satisfied by the property of every organism to be somehow *activated* whenever the basic balance (just representing the pursued coenaesthesia) is shaken from the outside or inside. The property to be activated is here meant, in a generic sense, as the faculty of temporarily changing one's state of relative quiet in response to certain actual stresses and then returning to the condition of quiet, once the *discharge* of activation has been obtained. The problem – and this is the core of our issue – is that the process *stimulus-activation-final discharge* is often completed in a non-linear way and having to face obstacles of several kind and level. This happens when the wanted discharge does not occur because of some impediment to the satisfaction of the need on which the original activation state depends. Therefore the organism remains in a condition distant from coenaesthesia until the discharge has been someway guaranteed thanks to the extinction of need. Let us here name this discharge *impasse* by the term *dystonia*, precisely intending any event that causes a block more or less localized within the organism and that thus prevents the return to the quiet of coenaesthesia by making a full discharge not possible. Schematically, we can express the three possible forms of dystonia considered in this paper as follows:



Figure 1. Generic activation lines

The first scheme represents the case in which two activated lines (A and B) converge on the same site S (named here *dystonic focus*) that cannot by its structure accommodate such a double entrance, thus becoming a point of activation overload generated by two competitors with consequent blocking of the discharge. The second scheme instead outlines the case of a *stagnation* of activation, that is a circumstance in which the current activation is not sufficient to open the way towards its discharge, determining thus a stalemate to be resolved. Finally, the third scheme offers the idea of an activation line that develops with multiple possible outlets towards the discharge excluding each other. In such a condition, the problem is just to give the current activation the possibility to *choose* which continuation to take for reaching its extinction positively. However we can express these three forms of dystonia also in logical terms so as to notice what it is exactly about by a different representation.

The first type of dystonia (symbolically put by d+) could be somehow fixed by a statement of the form:

$$[A \underline{\vee} B] \& (A \& B)$$

where V denotes the *exclusive disjunction* between the terms A and B while the entire statement expresses the fact that, given this reciprocal exclusion and despite it, both the terms are *true* or, in the language of our context, *activated*, by this pointing out a state of generic *overload* impasse.

The second type (d−) could be instead represented through the following sentence:

$$[A\&B] \,\&\, (A\&\neg B)$$

By this meaning that the global *truth* can be gotten only by virtue of the truth of both terms A and B and that instead only one of those is true. In the present language, it denotes that the discharge of the double activation line A and B is guaranteed only if both components are activated and hence that the activation of only one of the two terms generates a condition of activating charge stall.

The third type (d+/−) could finally be expressed by a proposition such as:

$$[A\&(B\underline{\vee}C)] \,\&\, (\neg B\&\neg C)$$

in which it is stated that the *truth* of a term A has to be accompanied by the truth of only one of the terms B and C – reciprocally excluding – and that neither the former nor the latter can be evaluated as true. In our language again, this is to say: if a line A is activated, A can find a unique outlet between two alternative activation lines B and C but it is not currently possible to decide which of the two is efficaciously *practicable* then the process gets stuck a state of indeterminacy with consequent impediment to the outlet itself.

So, on the basis of these schematic descriptions of what we here understand by *dystonia* as a *block* to the *discharge* of an ongoing *activation* within a hypothetical organism, we can now move forward by making some consideration on how the problem of pursuing coenaesthesia – and thus also overcoming dystonic events (has affected the structural evolution of the living organisms). In this sense, it should be noted that organisms, throughout their evolutionary history, have gradually developed inner structures with specific functional prerogatives to identify more or less localized *dystonic foci* and prepare automatic responses aimed at eliminating what exactly causes current difficulties in discharging activation and consequently restoring a condition of general equilibrium as required by troubled coenaesthesia (Ferraguti, 2011). These structures take shape by virtue of the ancestral disposition which cells (as elementary units of the life) have of being somehow activated but also of changing their response capacity depending on the conditions in which they are immersed. Therefore, in fairly complex organisms, certain cells have evolved by differentiating as to take on a very specific role in relation to other cells of the organism: the role of holistically organizing anti-dystonic vigilance (Bergson, 2015). In this way, these cells have developed also particular and functional capacities to receive and transmit information to each other and with respect to the other components of the organism. We are obviously talking about *neurons* with their more or less well-known bio-functional specificities. However, what is relevant here is that the emergence and evolution of neurons (as well as other types of cells after all) represent a process characterized by a progressive tendency towards the structural organization of the cellular components themselves into compartments having peculiar tasks integrated with those of the other compartments. Limited to our current interest we have to emphasize how such a tendency has led to the structuring of what can be generically called *homeostatic system* or *system of internal self-regulation of the organism's vital conditions.* Indeed, within this system, the fundamental needs of a complex organism clearly emerge in all their scope. This is to say that the system must: constantly monitor each organic region and each internal activity and autonomously provide for restoring and/or promoting acceptable homeostatic, i.e. non-dystonic, conditions. Homeostasis can be seen as the set of the processes through which the basic bodily coenaesthesia of an organism is pursued in its complexity, namely within a global systemic structure where different and inter-functional components coexist in a synergic and

multilevel perspective. Therefore, the homeostatic system, just roughly presented, is here taken as a complex of functions ruled by a framework of neurons and, as hypothesized in this paper, glial cells that collects data from the entire organism and then provides precise responses in feedback (and forward) aimed at varying or modulating each factor that can affect the homeostatic equilibrium (according to well-determinate biological parameters) and thus coenaesthesia. Schematically, we can set this system as follows (Lopez-Ortiz, 2023; Zhang et al., 2023):

$$\rightarrow/\supset/= \text{homSyst} \rightarrow/\supset/=$$

where $\rightarrow$, $\supset$ and $=$ respectively denote i) the neural ways, ii) the glial ways and iii) the humoral ways by means of which homSyst receives bits of information from the several parts of the organism and through which performs its own remote work of homeostatic adjustment.

Sensitivity, Memory, Awareness, Thought and Will

Therefore, if the homeostatic system represents a biologically definite example of how the organisms have evolved in structural complexity for better managing the basic need for coenaesthesia, gaining *de facto* some degree of freedom from an original condition of almost total passivity with respect to the pure matter, we can ever more clearly observe this tendency towards emancipation in other organic faculties that have also evolved in the perspective of the functional complexity aimed at pursuing the organic well-being in a holistic horizon. In this sense, we can certainly see how the development of diversified *sensitivity* to stimuli constitutes a demonstration of the attempt on the part of the organism to equip itself with more refined and effective tools to use in its constant effort in *dominating* the environment in order to draw from the latter what is necessary for its own internal needs. It is easy and intuitive to notice how the possibility of accurately distinguishing the mass of information coming from everywhere (both qualitatively and in terms of resolution) represents a force of strategic value in the battle having to be fought within a territory certainly not inclined to grant favours. The property to perceive something at a distance by sight or hearing, the ability to know the features of an object by touching or smelling it etc. are surely qualities which the evolution has progressively bestowed on organisms to improve their *being in the world* also making them predisposed to develop forms of coenaesthesia unknown at lower evolutionary levels.

But, alongside the diversification and refinement of the sensory skills, another fundamental faculty has gradually established itself. Faculty, after all, already primordially present in elementary life forms and somehow in inorganic matter too. We are talking about *memory* meant as property of retaining, storing and recalling lived experiences to exploit them again variously in the continuation of existence. In fact, it would not be particularly useful to develop powerful modes of sensory learning if all the pieces of information were lost in the actuality of the present moment. To memorize precisely means appropriating something so that it can be used later, perhaps even functionally manipulating and reorganizing the retained material according to one's potential. However, even memory as such would not be fully valorised if it did not combine with another basic property: the one that allows an organism to put itself as an individual organism to itself and by virtue of this become the real master of its own experiential dimension. This property is clearly *consciousness* understood as *awareness*. Very likely even animals (or at least those of a higher evolutionary order) are gifted with some form of awareness, but it is in the human beings that such a determination of individuality reaches its peak. Indeed, it is in humans that it imposes itself as the catalyst of experiences and holds itself in time and space making people *aware* not only of the experiences as such but also of the fact that those experiences are exactly theirs.

Continuing along this discussion, we can note that the affirmation of awareness is accompanied by the rising of that exclusively human faculty that goes by name of *thought*. It is just by thought, as higher faculty of processing information at various levels and in different

ways, that the human beings have further emancipated themselves from material contingency, and this is because thought represents that sphere in which it is possible to imagine and develop constructs without their contents being present in the empirical immediacy. As it is easy to understand, such a prerogative allows those who possess it to become somehow capable of preparing themselves for facing the future, and the events potentially contained in it, as best as possible. And this is precisely thanks to the asset of knowledge accumulated and developed in the past away from the empirical pressure. In the silver of freedom that thought grants, the individual can elaborate variegated and variously complex models as possible responses to any new challenges to be faced for safeguarding itself and its well-being, that is anyhow the manifest or latent target of every activity, even the most *abstract* one. Moreover, as mentioned above, thought has also made it possible to broaden the spectrum of field in which searching and getting global well-being (coenaesthesia) when compared to the primordial one focused on one's own simple organic nature. In any case, without dwelling too much on this analysis, it is enough to point out here that the activity of thinking truly establishes an evolutionary qualitative leap in complexity such as to offer humans the at least temporary opportunity to free themselves from the exclusive yoke of the organism-environment relationship.

The wonder of thought is intimately linked to a close ally, namely that of the *will*. Will is, by its very meaning, a propensity towards something rather than towards something else. Acting voluntarily means choosing among multiple action options, that is, means deciding whether to say *yes* to a certain option and *no* to another (or others) (Benini, 2022). This power makes will – that is always *decision-making* – a process rooted in awareness, meaning that the act of accepting or rejecting anything is a present act on which the individual is personally called to choose. It is evident that this typically human peculiarity, in its most evolved form, places the organism at an extremely high level of freedom, when compared to that of the mechanism of instinctual and automatic action. Schematically let us say that a voluntary act, of whatever specific type it is, can be defined as such if it can be traced back to a *tripartite* decision-making method.

Say *YES* or
Say *NO*, and if *NO*
SEARCH something alternative.

But what should we search something alternative to? What is the biological significance of this freedom of choice? First of all it should be observed that will also responds to the supreme principle of the sought after coenaesthesia for the organism in its wholeness. Thus, the decision-making will also comes into operation when it is somehow affected by the exigency to cope with some occurring dystonia. The core of question is that will, precisely because of the degree of freedom it possesses, comes out to be sensitive to a broader spectrum of dystonic forms than the one including only homeostatic forms faced by the autonomic system previously mentioned. As just said, will is close tied to thought (understood *lato sensu*), meaning that there cannot be any voluntary decision (i.e. a primary aware choice among multiple available options) without the intervention of the faculty that can actually carry out such a decision (making operation). So thought turns out to be functional to will, since the former ensures the latter its own sense of existence. Yet, at the same time, thought can only progress as *free thought* if it meets the criteria regulating any voluntary activity: i) say *yes*, ii) say *no* and iii) *search* alternatives. A construct of thought that comes out of this rigorous operational framework cannot be said *voluntary* and hence *free*. An *intuition*, for instance, is not in itself *voluntary*, since the *sub-threshold* (not conscious) work that supports it does not originate from a consciously decided act of searching something among different potential options. Will intervenes only once intuition has occurred by saying yes or no to it, but the voluntary mental process does not affect its previous genesis at all. We will see what all this entails later. For now, it is enough to remark that will – that is always *decision-making* will and *aware* will (*awW* in acronym) in the sense specified above – is the fulcrum of the highest degree of freedom which an organism can enjoy,

as it allows everyone to decide firstly whether accepting or not a *status quo* and, as a consequence of a refusal, to choose what to do as an alternative. Within will, in this respect, there is nothing *transcendental* or *superorganic*, since it too, like all other psycho-organic faculties, is subjected to the superior principle of the pursuit of coenaesthesia. Even will is activated by a dystonia, but the difference is that its freedom (acquired though evolution) makes it sensitive to forms of dystonia not only of a physical-homeostatic nature. Another characteristic to be highlighted right now, and then considered in more detail shortly, is that awW can come into play for dystonic events of two orders.

1) Dystonic events regarding *voluntary pure thought*. In this ambit a dystonia is caused by some content of thought that is not accepted in its entirety or in some part of it. In both cases, it gives rise to the following search for alternative contents that turns out to be overall acceptable, i.e. non-dystonic, for awW. Here we have an anti-dystonic *self-referential* search, that is, a search limited to the dimension of thought itself.
2) Dystonic events regarding contents of thought or organic states to overcome which a non-automatic but thoughtful action is required for changing the relation between organism and environment and thus modifying the flux of stimuli coming which the latter pours onto the former.

Dystonic cases of this type are the ones that cannot be overcome by means of *simple* homeostatic processes but rather require the use of appropriate *action patterns* for just modifying the relational state of organism towards environment. What is made possible by an aimed change defined on the basis of *procedural maps* and realized through more or less complex *motor sequences* decided by a voluntary act. But even dystonic events concerning contents of thought can require a certain modification of the organism-environment relationship in order to be overcome. It occurs when a mental construct, voluntarily developed or not, needs empirical confirmation (or denial) that are not available at present and that have to be sought in some *informational* context achievable only through *physical action*, understood in a very general way.

To conclude this section, we can say that evolution in complexity led to emergence of organic structures and functions with more and more sophisticated properties and tending to reach ever higher levels of freedom of organism from the strict situational contingency of its primordial relationship with environment. Anyway, we have to remark that also this phylogenetic pathway has to be ever interpreted inside the background frame of the tenet animating every living organism in its deep essence: the tenet of the search for well-being that holistically pervades each evolutionary level coexisting within it. Thought and will do not fail this bond, although they represent faculties – intimately related to each other – that guarantee organism a degree of freedom from basic environmental constraints not reachable through other functions actually available. Even thought and will pursuit coenaesthesia, but they do it by virtue of the sensitivity to dystonia that belongs to them and that derives from the (evolutionarily) acquired ability of considering environment not as an absolute dominator but as an instrument, necessary yes but still an instrument, to variously manipulate for obtaining one's well-being.

Will and Role of Glia in Voluntary Processes

In this section we present the first part of the hypothesis about the possible roles of *glia cells* (from now on simply *glia*) within the brain processes, hypothesis that exactly constitutes the core of the work developed here. To introduce the matter, as preliminary contribution, it seems to be helpful to briefly list the peculiarities of glia investigated so far in different experimental sites. It has to be emphasized that these prerogatives shift considerably the horizon within which such cytological components of the nervous system (and not) were confined until a few years ago, thus beginning to highlight capabilities and possible functions that are much broader

and more powerful than those of mere structures supporting and safeguarding the life of neurons.

GLIA:

SOME BASIC PHYSIOLOGIC AND FUNCTIONAL FEATURES AND RELATIONSHIPS WITH NEURONS

As said, a range of biologically important functions has always been attributed to glia but, on the other hand, recognizing a limited or not-existent role to these cells in determining the organic processes supporting the several psychic phenomena. This, despite the fact that glia constitute a quantitatively relevant portion of the entire nervous system. We are not dealing here with the now fairly well-known functions of mechanical, chemical and immunological protection of the nerve cells and nor with the myelination task which they are responsible for. We now attempt to briefly to point out a very important aspect of the glia properties only recently identified: i.e. the ability of glia to interact with neural dynamics and above all to respond, in their own way, to bio-molecular stimulations like neurons do and in synergy with these.

For convenience of exposition, we give a presentation in the form of a list of the factors, experimentally discovered, that underlie this *new* perspective concerning glia and their potential.

1) Glia, and in particular *astrocytes* with processes in perisynaptic areas, have the capacity to react, by becoming active, to the same neurotransmitters used by neurons to communicate with each other. This is to say that astrocytes are able to respond to neurotransmitters, in turn activating a sort of parallel *intraglial information transmission* (Haydon, 2001; Bezzi & Volterra, 2001; Nagai et al., 2021).
2) Communication within glia (astrocytes at least, as far as is known) occurs via calcium ions (Ca^{2+}) that are poured into the cells and distally diffused thanks a *gap-junctions* structure forming real connection networks among astrocytes (Nett et al., 2002; Berridge et al., 2003; Khakh & McCarthy, 2015).
3) Furthermore, glia communicate with each other by means of chemical substances, such as neurotransmitters themselves and various cytokines (overall said *gliotransmitters*), giving so rise to a real *interglial* communication system being actually still little known (Araque et al., 2014; Perea et al., 2009; Halassa & Haydon, 2010; Volterra & Meldolesi, 2005; Whealer et al., 2023).
4) Glia, activated by neurotransmitters emitted in and/or near synaptic spaces by neurons, have in turn the capacity of *modulating* the synaptic activity, in both a stimulatory and inhibitory sense. They do it in at least three different ways:
   i) by regulating degradation of neurotransmitters within synaptic clefts, in positive and negative sense;
   ii) by interacting with postsynaptic receptors by *agonistic* or *antagonistic* actions increasing or decreasing the responsiveness of postsynaptic neurons and (Iino et al., 2001; Murai et al., 2003; Stork et al., 2014; Chung et al., 2015; Allen & Eroglu, 2017);
   iii) as regards astrocytes with perisynaptic processes, by occluding or opening synaptic spaces through mechanical movement of lengthening or withdrawal of their extensions. (Oliet et al., 2001; Piet et al., 2004; Lehre & Rusakov, 2002; Hirrlinger et al., 2004).
5) Schwann cells and oligodendrocytes too – i.e. glia that envelop the axons of neurons in central nervous system, forming a layer of myelin around them, show a similar capacity to

respond to the activation state of neurons (specifically of axons) to which they are structurally and intimately connected (Reist & Smith, 1992; Robitaille, 1998).

If this is what emerges from the laboratory research carried out so far, then it makes sense to hypothesize the existence of an effective and synergic neuronal-glial communication network that operates to make possible the occurrence of many of those phenomena that have always been considered as phenomena exclusively determined by the activity of neurons. The assessment of the properties of glia listed above is something that really opens up a world of questions and suppositions about the precise potential that such cells have. A world of hypotheses that as such have to be not only outlined in a heuristically plausible way but then also subjected to a verification pathway in appropriately defined experimental contexts. Following exactly a hypothetical approach, we try to imagine possible glial roles played, with diverse purposes, in the processes organized by will and partly performed also thanks to the contribution of the autonomic mechanisms. outside the control of aware will – of more ancient phylogenetic origin.

Recalling what has been already exposed, we say that our aware decision-making will awW intervenes when:

a) a certain dystonia reaches awareness as a dystonia to which will is sensitive and
b) it turns out to be necessary to operate according to a basic procedure that involves a *yes* or a *no* and a search among different options to choose from in an attempt to overcome the dystonic state.

Any anti-dystonic action that does not start from a conscious act and that is not attributable to the tripartite intervention scheme has to be here considered not-voluntary.

We also have to distinguish, as previously mentioned, two planes for possible intervention by awW:

I) the plane of pure thought, where one operates in the self-referential sphere of thought itself and
II) the plane that affects organism and its relationship with environment, where a change in this relationship is just required and where such a change can only be carried out through some specific sequence of action decided by will itsel

We now deal with the two planes separately and begin with the one of pure thought.

Pure Thought and Voluntary Regulation

Firstly, we have to clarify that pure thought taken into account now is precisely *voluntary* thought, namely the one whose course is controlled by will according to its tripartite operational criterion. A spontaneous fluctuation of contents or an intuition are not voluntary thoughts. Voluntary thought begins with an *aware acceptance* of a content or with its *rejection* that then gives rise to a *search* aimed at finding something that can satisfactorily replace what has been rejected. It can be intuitively grasped that the aware *rejection* of a thought content (or part of it) occurs when *awareness* identifies some form of dystonia existing in that content.

Let us see how this process can be represented in a simple and schematic way, that is, without claiming to rigorously follow all that happens at the brain level when a thought is developed. So, if we put P as denoting a (more or less complex) thought content and imagine that P is felt for some reason as *dystonic* by awW, then we can outline a hypothetical voluntary response dynamics as follows.

1) $P = \langle P_1 \ldots P_n \rangle$ where every P_x is a part of the global content P that is the object of *dystonic* perception;
2) P_x^+ is a part of P accepted by awW, i.e. a part of P to which awW *says yes*;
3) P_y^- is a part of P rejected by awW, i.e. a part of P to which awW *says no*;
4) $P_x^+ \approx P_y^-$ denotes a hypothetical relation linking P_x^+ to P_y^- (and/or vice versa).

Now, the problem for awW is to replace P_y^- with some other P_z (currently not present in awareness) such that $P_x \approx P_z$ is not the origin of dystonia and in this way obtain a content P* that turns out to be *complete* and *not-dystonic* with respect P_x and P_z. How can such a replacement be achieved? Certainly, by a search for something that is not yet possessed in awareness. If an anti-dystonic replacement occurred immediately – without any preliminary search – then the ongoing voluntary process would stop and an *intuition* would arise. This contribution of intuition would in fact be accepted or rejected by will, but it would not emerge from the same voluntary process that, upon the rejection of a content, should instead open up an effective search among diverse potential options without any initial predisposition. But where and how has this search be performed? Here is the core of the issue and from here we start with our hypothesis. Let us imagine that awW decides to search, within the *space of thought contents*, for what it needs to overcome the current dystonia and to do so compatibly with what it has accepted, i.e. the part P_x. According to the picture of the voluntary thought which we have just exposed, we have to assume that awW does not *a priori* know what precisely can be suitable for its goal and therefore it must, in a certain sense, *rummage* in the memory space – or in a part of it relevant to the content P_x from which the search starts – to probe among the more or less solid memory tracks contained therein and to ascertain whether some element with the wanted anti-dystonic characteristics can be extracted from them. To respect the criteria of a search path conceived on these bases, awW has to proceed by activating widespread attention but not focused on anything specific. Just so we are faced with an act of voluntary free thought. From a physiological point of view, we can imagine that the search set in motion by awW (as *awW over STC*) occurs in a, *mutatis mutandis*, modality similar to the one of an *attentional arousal*, i.e. as a broad but not targeted solicitation on the space of thought contents (STC). This van be done by activating many contents simultaneously *sub-threshold*, namely without anything being brought to awareness, in such a way that some potential option can become actual (i.e. come to awareness) in absence of any preliminary preference. The unique aware a priori goal is to find some thought content suitable for the wanted anti-dystonic replacement, the rest of the dynamic has just to take place below the threshold of awareness. Just in these terms we can have a free and voluntary thought process.

At this point in the narrative, we introduce what is intended to be a hypothetical suggestion on the *collaborative* role of glia in arousal searching within STC. So, if we recall that glia: i) are activated together with the activation of neurons to which they are proximal and ii) communicate with each other, we can start with the hypothesis by supposing that glia in our situation are precisely activated in harmony with neurons that sub-threshold activate STC, following them throughout their activation paths within STC itself. On this basis, we now try to construe a theoretical representation of the process, triggered by awW and originating from the situational premises described above, as we imagine it.

a) P_y, or rather, the relation $P_x^+ \approx P_y^-$ is *voluntarily* (thus consciously) inhibited. Therefore, the content P_y is not included in the portion of STC affected by the arousal activation.
b) All the pathways $\rightarrow/\supset$ – i.e. all the neuronal-glial pathways that are activated in parallel – start from P_x (thought content conserved in awareness) with the same level of arousal activation on STC.
c) The several pathways begin to branch off in various directions, all with the same initial activation intensity, until some of these them – for reasons unrelated to awareness – increase their own level of activation.
d) The strengthening of a specific double pathway $\rightarrow/\supset^*$ (or more than one) in its turn promotes interglial communication between glia belonging to $\rightarrow/\supset^*$ – i.e. to some strengthened pathway – and those belonging to pathways still activated at the minimal arousal level.

e) Glia of $\rightarrow/\supset^*$ communicate to glia of *weaker* pathways that *the right direction has been taken and search is aiming at the wanted goal*.
f) Once received the message, glia of not strengthened pathways *agonize* on the pathways with higher activation level and do it by *inhibiting* just the pathway to which they belong, as in a self-sacrifice consumed for creating *silence* around pathways $\rightarrow/\supset^*$ and increasing their activation level even more.
g) Thus, as the process progresses, the number of pathways $\rightarrow/\supset^*$ (strengthened pathways) decreases, thanks to the sacrifice of the *weaker* ones, until a few pathways (or even only one) reach(s) the necessary activation level for bring to awareness some content P_z which they have in fact identified through their increasing activation state. So, in awW the *new relation* $P_x \approx P_z$ emerges and awW returns to the position of having to decide by a *yes* or a *no* about the global new thought content P*, with $P_x \approx P_z$ belonging to P*, formed throughout the search phase.

We can conclude that the synergic action of:
1) silence of the previous relation $P_x \approx P_y$ with maintenance of P_x;
2) progressive increasing in activation of some pathway $\rightarrow/\supset^*$ that delineates a very specific direction ending in P_z and
3) parallel progressive extinction of weaker pathways guided by interglial communication (Even Jones & Greenough, 2002; Santello et al., 2019).

determines the additional amount of activation required to deliver $P_x \approx P_z$ to awW.

But now the question is that, if this dynamics is plausible, then the role of glia in voluntary thought turns out to be, at least hypothetically, anything but secondary or even not-existent. The agonistic action of glia independent of pathway $\rightarrow/\supset^*$ that supports $P_x \approx P_z$ – an action required just by glia of $\rightarrow/\supset^*$ and consisting in completely *silencing* the weaker pathways previously activated sub-threshold for broad-spectrum search in arousal – becomes a fundamental intervention in order to find some suitable replacement for the portion of ongoing thought from which dystonia arises and consequently search begins. It is a fundamental intervention for more than one reason due to both the particular condition of arousal activation in which the hypothesized search is performed and the properties themselves of the two types of activation pathways – the neural one and the glial one – involved in this dynamics. First of all, we shall keep in mind that an arousal activation is a widespread activation but such that it remains homogenously contained on the entire area and this precisely so as not to offer any privilege in initial activation to any activated direction. Well, our hypothesis also contemplates that the activation level of a direction can increase or decrease under certain conditions and these essentially establish that a pathway loses its amount of arousal activation, just from the beginning of the pathway itself, only when other pathways show to be more *reliable* for achieving the goal – i.e. to give awareness some substitute content being contextually anti-dystonic. This situation occurs when certain pathways are able to progress more easily in their internal connections while others remain *mired* in activation levels being too weak to move forward, giving so rise to a sort of localized *activation impasse.* The purpose, in these conditions, is exactly how to subtract amount of activation from the *sterile* pathways and channel it towards the *more vigorous* ones. An operation of this kind can be performed by inhibiting the formers right from the origin and thus ensuring that their amount of arousal activation is directed to the latters, making them even *stronger*. But to carry out such an operation, glia, by virtue of their morphologic-functional properties, seem to be much more suited than neurons. Firstly, glia can communicate with one another even very distally and above all ubiquitously. Moreover the glial communication is structurally more *agile* and *flexible* than the neuronal one conditioned, as it is, by the rigidity of synaptic transmission. For these reasons, the task of re-dosing the total

activation quantity among different pathways appears really to be more a competence of glia than of neurons. It should also be observed that neurons, being the components of the activating channel that brings contents to awareness, are structured to operate on an *all-or-nothing* basis. This is to say that, if neuronal pathway is *more promising* than another – in the sense of having a more robust activation tendency – then it:

I) Either immediately brings its result to awareness, *nipping* any search in the bud when instead it has to start from a set of option with equal potential;
II) or leads to nothing since it remains stuck at an activation level that can be higher than others but not such as to exceed the threshold of awareness nor can it progressively reach this condition.

Based on these considerations, it is plausible to state that just a communication network external to neurons, but functioning in harmony with them, is the one having the best tools to perform a task of this type. More generally, always according to this hypothetical dynamics, we can conclude that voluntary (or voluntarily guided) thought has nothing *creative* in the sense that it is not identifiable with the intuitive *exploit*. Intuition is not bond by any search process since it does not derives from a set of potentially *equiplausible* options from which some (or only one) is chosen through a defined procedure. An intuitive content arises spontaneously and is what it is and will intervenes, deciding its fate by a yes or a no. However will, by search which it promotes, can predispose thought to carry out operations that would otherwise not be performed. This is because such operations originate from a preliminary rejection of something that consequently requires to be replaced. And, as conjectured, glia play a determinant role in this peculiar process precisely by virtue of those properties which they seem to possess on the basis of what emerges from the experimental investigations conducted up to now.

However, the hypothesis about the glial role within the process of voluntary thought can be further expanded. By this we mean that glia, in their functioning also independent of specific neural pathways, could contribute to the formation of a thought by acting externally to the exact brain area in which that thought takes shape. But, to deal with this topic it is helpful to preliminarily establish a couple of concepts of which we now provide a summary overview. We want specifically to clarify what we here mean by *attention*, *aware attention* and *working memory*.

Attention in its Forms

Each content of awareness, as we know, takes up the attention of the moment in a more or less catalysing way. When a content becomes the object of attention, the latter focuses on it while contemporaneously tending to exclude anything else that could compete for access to awareness. The fact that the focus of conscious attention requires, for being kept, to exclude everything not falling within this focus depends on the very limited dimension of attentional awareness. Therefore, in the case of the process of voluntary thought just considered, one has the problem of reserving the (scares) space of aware attention to that thought content about which the *revision* actioned by will is taking place. Anyhow, to carry out this revision, as we have seen, it is also essential to resort to the not-aware area of thought contents (STC) within which search in arousal condition is performed, as well as it has been described. This entails that, besides an aware attentional focus, there is a parallel not-aware one extended over STC involved in search. We can define, though a little licentiously, the union of the aware attentional focus and the sub-threshold one as *working memory*, referring to the particularity that in our search procedure – i.e. in the type of work investigated here – some elements of the problem have to be held firm in the limited space of aware attention but having the possibility of finding others maintained below the threshold of awareness at the appropriate step of the procedure itself.

Starting from these defining premises, we can now extend our hypothesis about the contribution of glia in dynamics of voluntary thought also examining what glia could do to guarantee working memory, as we have defined it, to operate in the best condition. The

question is: how can awW takes advantage of the help of glia to protect the work it is overall managing from potential and/or current *disturbing factors*? In this respect we can formulate the following conjecture. Will, that is a high and articulated function of an evolved organism and just for this reason also in need of greater independence, could delegate certain external support tasks for its activity to less evolved but more automated functional centres. So, it seems to be conceivable that awW can make use of the autonomic regulation mechanisms developed within the homSyst structures – that as such have the original task of governing homeostasis – for creating a sort of *protective bell* around working memory. Namely, the need of awW to keep both aware and sub-threshold attention on well-determined contents and thought areas (i.e. on the working memory field) could be satisfied by the inhibitory autonomic mechanisms exploited with the aim of blocking any disturbing element potentially threatening the sites to be protected. If that is the case, the inhibitory autonomic mechanism have to monitor stimulations coming from various regions of organism and that can be identify overall in sensory stimuli and spontaneous mental contents interfering with the (aware and sub-threshold) contents involved in the ongoing search. How can these mechanisms succeed? Using neuronal inhibition where possible and resorting to the precious help of glial inhibitory action where necessary. But why is glial recruitment something plausible in this procedure? The answer is: because glia have the property of being activated and communicating with each other *ubiquitously*. That is, these cells, once activated in certain points, can carry information distally, over a wide range and more fluidly than how neural transmission rigidly conditioned by its synaptic structure can do. Having to simultaneously to control many sources of possible disturbance, a *weapon* with these characteristics can be very effective for the purpose. In support of our thesis we have some experimental works which exactly corroborate the idea of a distal inhibitory action of glia correspondently to an attentional current focus. Specifically, these findings show how an attention content, immersed in a noisy environment from which a large quantity of disturbing stimuli comes, can be isolated also by the intervention of protoplasmic astrocytes performed in a selective way. According to what has been observed, astrocytes, through a distal release of ATP – rapidly converted to *simple* adenosine outside the cell –, cause a short-term depression of synapses in *strategic* points of the sensory pathways which target the entorhinal cortex and CA_1 and CA_3 hippocampal strati, so as to really facilitate the contextual retention of only the desired object. These evidences support, among other things, the hypothesis concerning a structural-functional organization of ensembles of astrocytes (and perhaps also other glial cells) which would thus constitute true competence networks equipped with a rather refined communication code. On the basis of these preliminary notes we can now formulate the final part of our hypothesis about the second role of glia in the process of voluntary thought. Similarly to what has been done for the first hypothesis, we try to imagine the dynamics in question just as it could develop step by step.

a) Will, or rather, awW focuses on a thought content P that has to be somehow changed.
b) Search is activated in STC, as described above.
c) The scope ok working memory is here given by aware attention fixed on P and sub-threshold attention covering the portion of STC affected by search.
d) awW recruits the autonomic inhibitory mechanisms of archaic origin to isolate

area of aware attention U area of sub-threshold attention

from the rest of organism, where by *rest of organism* we mean any organic (and mental) site from which disturbing elements for working memory can come.
e) Isolation work has hence to be performed in such a way as to intercept any source of disturbance D – coming from sensorial, emotional or mental areas – that arises as D → WM, i.e. as a potential direct *contaminant* of the working memory spaces.
f) The process occurs automatically – namely it is not controlled by awW – thanks to the use of different inhibitory means, all aimed at inhibiting not the stimulations as such but, functionally, the channels that can bring them to working memory. That is,

$$D \rightarrow^{inhib} WM.$$

In this important and demanding operation, as said, glia could offer a relevant contribution. They could receive the order from awW to proceed – in the silence of their evolutionarily consolidated automatisms – to stop every foreign element that approaches the working memory space. A bit as if they were immune agents with the task of guaranteeing that voluntary thought can develop in an *aseptic* condition. Glia, by their nature, seem to be really suitable to carry out such a particular function. This holds both for their flexibility in being activated and for the property to communicate distally and everywhere without too many structural constraints. As it is easy to imagine, all this represents a significant advantage when a wide-ranging work is required. So, we can complete the previous symbolic expression as follows:

$$awW \rightarrow {}^{(inhib)}\supset \ldots. \supset D \supset_{\rightarrow}{}^{inhib} WM$$

thereby meaning that: awW, by starting the arousal activation, also actives proximal glia; the latters begin to communicate distally; when the message reaches glia close to active neuronal centres that can bring stimuli to the areas of WM, these glia produce their inhibitory action. How glia can perform such an operation is clearly an issue to be carefully studied. About that, we can here hypothesize that glia exploit their mechanical ability to physically occlude synapses. But there is even the possibility that they use other means, such as the massive release of neurotransmitters degraders or substances that generate an antagonist effect at the level of postsynaptic receptors. These are all operations which glia can perform by virtue of their functional patrimony evolutionarily acquired.

Well, glia, according to our global hypothesis, could thus fulfil two fundamental tasks in the activity of voluntary though. They can have:

I) an agonistic function in arousal search over STC – as seen above – and
II) an antagonist (purely inhibitory) function in isolating the areas of WM involved in the ongoing thought.

As it has already been highlighted, each of these hypothetical suggestions is derived from the basic morphologic-functional properties of glia which we currently know. But whether those properties are such as to support the hypothesized dynamics in factual reality is a matter to be verified experimentally. In particular, as regards the first conjecture, one should test how actually the intra-and-interglial communication occurs, that is, how crucial information to bring out a content within the process of arousal search is conveyed among glia. In essence, one should investigate which *code* glia belonging to a *strong* pathway $\rightarrow/\supset^*$ use for communicating to other glia, engaged in other arousal search pathways, to interrupt their action and turn off the *weaker* pathways so as to allow the amount of arousal activation recovered from this silencing to converge on the *most promising* pathway – in the sense specified above. In short, the topic of interglial communication is a question of primary importance that has to be dealt with in experimental contexts in the most serious and rigorous way possible. Here we can only give some summary idea on how the investigation could be directed. For instance, as far as the issue of the glial communication code is concerned, we can heuristically suppose that the *informational core* is provided by the initial slight over-activation of the pathway symbolically denoted by $\rightarrow/\supset^*$ – and named *strong pathway* – that is delineating the relation $\approx$ between the aware content P_x and the still sub-threshold content P_z (Araque et al., 2014; Tognatta et al., 2020; Doron et al., 2022). Given this assumption, it should be hence tested whether the over-activation of a specific site is accompanied by the deactivation of other specific sites, all included in the WM area, or, in other words, whether there is some temporal and topic correlation between the phenomenon of over-activation of the pathway $\rightarrow/\supset^*$ supporting $P_x \approx P_z$ and the one of decrease in activation of other pathways active in arousal search. Some confirmation in this sense would be a corroboration for the hypothesis of a joint intervention based on

communication to favour a neuronal-glial pathway over others. But, a further relevant aspect should be experimentally investigated. Namely: what is the means by which glia transmit the message? Here the problem would be to understand whether, for example, this transmission:

I) is realized through chemical substances with a distal localized effect, similarly to what occurs in communication via hormones or cytokines, or

II) is based on some dynamics of physical nature by virtue of which a quantitative disparity in something between two points determines some particular event in one of these points. In this case, it is possible that a greater intraglial amount of Ca^{2+} in glia of the over-activated pathway $\rightarrow/\supset^*$ induces glia of pathways with less Ca^{2+} to trig the inhibitory self-aimed process.

All material that would be interesting to explore further in the appropriate places. Here we add only that, however the interglial transmission of the message occurs, there should be some minimal time lag between the moment of the over-activation of a particular pathway and the starting moment of arousal search in which the level of activation has to be the same for all. Only in this way it would be possible to validate the thesis about a sub-threshold search among several a priori equiplausible options from which some (or one) can then emerge and reaches awareness.

On the other side, an experimental approach would also be opportune for the hypothesis on the role of glia as an insulator of the WM areas. Indeed, even for this phenomenon it should be ascertained whether there is some temporal and topic correlation between the activation of a voluntary thought (like the one previously outlined) and glia close to the WM areas. Furthermore, as above, it should be investigated the precise nature of the code by which it is communicated to glia where to intervene and what to do – i.e. prevent the access of disturbing elements to the WM areas –. Is this function carried out by substances or molecules that delimit the space to be protected and that have the power to induce glia to behave in a certain way? *Mutatis mutandis*, a bit like what occurs for the cellular *major histocompatibility complexes* (MHC) that activate T lymphocytes. Or, also at this level, is this glial function governed by some physical factor? Perhaps a dynamics by which the massive activation of glia proximal to the WM areas, with consequent increase of intraglial Ca^{2+}, determines a behaviour in distal glia exactly aimed at inhibiting the pathways accessing WM, where the insurmountable limit for these is just signalled by the amount of activation that draws the border? All this, as emphasized, without necessarily touching on the contents or stimuli as such but only on the pathways that could lead them to the areas recruited by WM.

We have previously said that glia could also play a dual role on another plane on which awW intervenes as promoter of changes in anti-dystonic function. Therefore, even in this dimension the issue of glial communication turns out to be, as we will see shortly, absolutely fundamental. We are talking about the plane of voluntary changes that require some modification of the relationship between organism and environment, i.e. changes that can be done only through *action* and thus *movement*. In the next section this topic is dealt with.

Voluntary Changes of Organism-Environment Relationship Through *Action Patterns*

Not every type of dystonia can be overcome by means of mechanical automatisms of homeostatic regulation or treated in the self-referential sphere of pure thought. There are many situations in which overcoming a dystonia – that consists in allowing an activation discharge remaining hindered for some reason – is possible only by changing the mutual relationship between organism and environment so as to modify the sources of stimulation of the latter on the former. Events like these can occur both with regard to an organic dystonia that cannot be regulated by homeostasis and for a thought dystonia that cannot be overcome in the closed dimension of the thought itself. In these circumstances awW has to act in a radically different way in comparison to the one exposed above. To handle the problem, awW has to adopt some

action strategy that is *previously* judged as suitable for producing, at the end of the action, the relational change between organism and environment conjectured exactly to resolve the current dystonic impasse. Differently from the sphere of pure thought, where the possible anti-dystonic solution is realized simultaneously with the development of its search, here there is a *preventive* search of an action path that, once completed, should lead to the wanted goal. In other words, we have to do with a bipartite procedure divided as follows:

I) the *preventive* search of a *map*, consisting in an *action pattern*, to be followed and
II) the implementation of the decided AP at the end of which its real anti-dystonic effectiveness is verified.

Now, to develop the matter just presented it is necessary to clarify what has to be meant by *action pattern* as content of a *map* indicating how to change a current relational state between organism and environment into another with specific wanted qualities.

Action Patterns: What they are and How Much They Constitute Anti-Dystonic Maps

An action pattern (from now on simply AP) has to be meant as a series of steps that leads to a modification of the relationship between organism and environment. Each step within an AP is precisely a more or less complex action that involves a *movement* from which a positional change of organism derives. Moreover, in an AP, each step, i.e. each action, is defined in a *peremptory* and *univocal* way, in the sense that it is preventively identifiable without any possibility of being changed except by leaving the step itself or the AP of which it is a part. An AP is thus a sort of *packet* of actions completely determined in their execution. Without dwelling too much on a matter that is of secondary importance here, we can roughly say that a step/action of an AP can essentially be of two types:

1) an automatism – i.e. a motor modality learned and applied mechanically, or
2) a more or less complex operation conceived in thought in a conjectural form, as an abstraction or generalization with respect to experiences acquired over time etc.

What is relevant to point out is that each action is understood as something fully defined that, once started, continues autonomously or, if we prefer, algorithmically according to its dynamical model. This entails that the whole AP, formed by a series of connected actions meant in this way, is nothing other than a broader action itself, where each internal step is always marked up by a positional change deriving from a *movement* and determining a *modification* of the organism-environment relationship.

After having clarified these aspects, and before continuing in the discussion about the APs, we need to introduce a couple of *technical* definitions.

[*Def.* 1]

Let us put T = $\rightarrow/\supset$ for denoting the neuronal-glial pathways (or circuit) supporting the thought "T", i.e. a specific *mental* content.

Let us put bE = $\rightarrow/\supset$ for denoting the neuronal-glial pathway (or circuit) supporting the bodily experience "bE" – where *bE* just stands for *bodily experience* such as a sensation or a percept – depending on a current stimulation flux from environment towards organism.

[*Def.* 1.1]

Let us say that T is the *mental representation* of bE when

$$\{\neg T \ U \ bE\}_d$$

that is, when, for every T* such that $\{T^* \ U \ T\}_d$, we have $\{T^* \ U \ bE\}_d$. In other words, the simultaneous and contextual occurrences of the mental content "T*" and the bodily experience "bE" generate a dystonia between thought and bodily state.

[*Def.* 2]

Given $bE_1 \ldots bE_n$ activations supporting bodily experiences, let us put

https://doi.org/10.46627/sipose.v6i1.409

$$\underline{Org} = {}_1U_n bE_x$$

(i.e. the union of the activations supporting the bodily experiences "bE"$_1$ … "bE"$_n$) as *configuration of state* – implied: … *of a hypothetical organism org at a hypothetical time t* –.

Hence Org denotes the global bodily activation state whose experiential effects are present to an individual's awareness and that describes the relationship between this individual's organism and environment at a given moment.

[*Def.* 3]

Given $\underline{Org} = {}_1U_n bE_x$ configuration of state and $T_1 \dots T_n$ mental representations of $bE_1 \dots bE_n$, let us put

$$Org = {}_1U_n T_x$$

as *mental configuration of state Org*.

Hence Org denotes the set of the activations supporting the thought contents that mentally describe the aware bodily state of an individual at a given moment.

[*Def.* 4]

Given Org and Org° mental configurations of state, let us put

$$Org < Org° \text{ (Org° } \textit{includes} \text{ Org or Org is } \textit{included in} \text{ Org°)}$$

when $\{\neg Org° \cup Org\}_d$, i.e. when for every Org* such that $\{Org^* \cup Org°\}_d$ is also $\{Org^* \cup Org\}_d$. Or, similarly again, Org < Org° when Org° represents a *broader* mental configuration of state than Org.

Returning to the topic regarding APs, we can say that an AP is delimited by an Org^{in}, that represents the input configuration, and an Org^{out} that instead is the output configuration resulting from the various manipulations performed in the steps that univocally constitute AP. Therefore, by extension of the concept of *inclusion* expressed by the relation < defined in def. 4, we can put that, given an Org mental configuration of state and an AP:

$$Org \textit{ is included} \text{ in AP when}$$
$$Org < Org^{in}AP$$

i.e., Org can be subjected to the series of changes established in AP when Org is included in the input configuration of AP or, in other words, when Org is a *case* of the more general Org^{in} from which AP starts.

We now complete the framework of our *technical* definitions by setting the notions of *sequence of action patterns* and *anti-dystonic sequences of action patterns.*

[*Def.* 5]

Given $AP_1 \dots AP_n$ action patterns, let us say that

$$AP^* = AP_1 \dots AP_n$$

is a *sequence of action patterns* when, for every AP_x and AP_{x+1}

$$AP_x Org^{out} < Org^{in} AP_{x+1}$$

that is, when every AP_x is concatenated with the next AP_{x+1} through the relation of inclusion < that defines the transition. It has to be noted that, while each internal step of a certain AP is characterized by a change requiring some action, the transition between two contiguous APs is determined by an *inclusion*, namely by the request that the result of the previous AP is tractable according to what the first step of the following AP establishes.

It now remains to be seen how the notions of AP and sequence of APs can be exploited for defining an anti-dystonic map aimed at solving a real dystonia occurring in some real organism. We have to reiterate that an anti-dystonic map, in our view, is a procedure decided *in advance* (*a priori*) by awW, on the basis of specific evaluations, and then currently implemented in the expectation that it will provide the wanted result. So, we give the following definition.

[*Def.* 6]

Given a sequence AP* = AP_1 … AP_n of action patterns, given a real dystonia (d) in organism with configuration Org (symbolically $Org_{(d)}$) and given the mental configuration Org′ of Org′ such that for Org′ dystonia (d) does not occur – i.e. Org′ is $Org'_{(non\text{-}d)}$ and Org′ is $Org'_{(non\text{-}d)}$ –, let us say that AP* is an *anti-dystonic sequence for* $Org_{(d)}$ when the mental configuration $Org_{(d)}$ of $Org_{(d)}$ is:

a) $Org_{(d)} < Org^{in}AP_1$ and
b) $AP_nOrg^{out} < Org'_{(non\text{-}d)}$.

This is to say that AP* constitutes an anti-dystonic map for $Org_{(d)}$ when it is formed by a sequence of more or less complex operations that mentally leads $Org_{(d)}$ to change into a configuration for which dystonia (d) is not more active. This can occur thanks to a variously modified organism-environment relationship and regardless of any real connotation of the new configuration that is not influent with respect to the dystonic site d.

The idea behind a dynamics conceived in this way is exactly that, in delineating a map based on an AP*, it is necessary:

1) to abstract from everything that is inessential to the goal to be pursued;
2) to use well-defined operating methods with their *instructions* as punctual and unambiguous as possible; that can be obtained just by choosing an AP* that is rigorously structured in its internal dynamics and found from mental material already learned through experience or elaborated by thought;
3) to ensure that, at the end of the path followed step by step, the foreseen goal is achieved, i.e. that the transition established by AP* leads a certain initial configuration to change so as to take on the features of a different and searched configuration of state

Nevertheless, in order to implement the notion of anti-dystonic sequence AP* for $Org_{(d)}$ that has to be sought, it is necessary to frame it into the real context of a search carried out by knowing only the starting point and the final point, that is, $Org_{(d)}$ and $Org'_{(non\text{-}d)}$ respectively. This is to say that, in the current search for a specific AP* for some $Org_{(d)}$, it occurs that the several steps of AP* are not precisely determined from the start, i.e. that, once a step has been reached, the next ones can be only overall conjectured but without an exact inner scan. In similar circumstances, search encounters some state like the one defined below.

[*Def.* 7]

Given Org and Org* mental configurations, let us put that Org* is a *goal* of Org (symbolically Org $\rightarrow/\supset {}_gOrg^*$) when there is some sequence AP*′ such that

$$Org < Org_1\ AP^{*\prime}\ Org_n = {}_gOrg^*$$

where AP*′ is a sequence whose components AP_1 … AP_n cannot be distinguished from each other.

The sense of a such *limiting* definition for the context of a real search is to fix the idea that, in the preventive (a priori) condition in which the search process works, it can identify a pathway in its generality but not know such a pathway in its details. On the other hand, if it were not so, search would be accomplished right from the start.

Based on this series of definitions, the next issue we are going to deal with is how awW can conduct search for an anti-dystonic AP* once a dystonia has emerged and has emerged as a dystonia that can be overcome by a change of the current relationship between organism and environment. Here too we try to identify possible roles of glia in performing the task and here too, naturally, we propose everything in purely hypothetical terms.

Search for an Anti-Dystonic Sequence Ap* and Role of Glia

To face the topic, we adopt a schematic approach, in which each phase, starting from the initial condition that originates search, is presented as a stage of a linear journey.

https://doi.org/10.46627/sipose.v6i1.409

1) The starting condition is given by a configuration of state $\underline{Org}_{(d)}$ denoting a current dystonic state that has reached awW.
2) Once registered the presence of a dystonic focus that can be overcome through a change of organism-environment relationship, awW begins its work by setting the goal to be achieved: a configuration of state whose mental configuration is given by $Org'_{(non\text{-}d)}$, i.e. a configuration for which the dystonic focus (d) is not active.
3) The first passage of the anti-dystonic task consists in *searching* some sequence of *action patterns* AP* that turns out to be now mentally suitable to achieve the target after it has been put into practice.
4) Therefore, the two elements on which *attention* of awW – i.e. the *aware* attention – is focused are $Org_{(d)}$, that is the mental configuration correspondent to $\underline{Org}_{(d)}$, and $Org'_{(non\text{-}d)}$.
5) Search for some anti-dystonic AP*, suitable to lead $\underline{Org}_{d}$ to become like some $\underline{Org}'_{(non\text{-}d)}$ whose mental configuration is just $Org'_{(non\text{-}d)}$, has to be performed within the portion STC* of STC (space of thought contents) in which more or less elaborated APs already acquired are conserved.
6) WM (working memory) of awW is thus represented by the space of aware attention – focused on $Org_{(d)}$ and $Org'_{(non\text{-}d)}$ – and the space STC* on which the *arousal* (*sub-threshold*) search has to be performed.
7) From the contents in awW search in STC* begins. As seen above, the arousal search is such that, in it, each neuronal-glial pathways $\rightarrow/\supset$ starts with the same activation level – precisely because only in this way search comes out to be really voluntary and free and not somehow *predetermined*.
8) At this point our hypothesis on how glia could intervene in this search starts. So, when a certain pathway $\rightarrow/\supset$ encounters some AP such that $Org_{(d)} < Org^{in}AP$ and $APOrg^{out} \rightarrow/\supset {}_{g}Org^* < Org'_{(non\text{-}d)}$ – i.e. $APOrg^{out}$ turns out to be aimed at a goal Org* such that it is just a case of target $Org'_{(non\text{-}d)}$ of search – glia belonging to this pathway *communicate* to other glia that "*search has found a possible way for leaving the starting condition in an useful way*" so that glia belonging to *still sterile* pathways *inhibit* those pathways themselves, allowing the amount of arousal activation released to converge on the first pathway that becomes *stronger* – symbolically $\rightarrow/\supset^*$ – and search to continue from AP that becomes AP_1.
9) The process goes forward *recursively* for every AP_x on AP_{x+1} through the progressive extinguishing of the *fruitless* pathways and the parallel strengthening of the more *promising* ones. Search ends (successfully) when, for some sequence … $AP_xOrg^{out} \rightarrow/\supset {}_{g}Org^* < Org'_{(non\text{-}d)}$, $AP_xOrg^{out} \rightarrow/\supset {}_{g}Org^* < Org'_{(non\text{-}d)}$ reaches an activation level that at least equals the threshold of awareness – even if the final part of AP* still remains in an internally *unfixed* form so that AP* remains as an AP*'.

Therefore, the process represented in these nine stages brings to awW a sequence AP*' that appears to come as close as actually possible to expectances, i.e. a complete AP*. At this point awW is the position to decide whether to accept AP*' and start the second step of the anti-dystonic task – i.e. physically implement AP*' – or reject it and restart with a new search.

In a similar way to what has been done previously, here too we hypothesize that the neuronal-glial pathways $\rightarrow/\supset$ in play are *strengthened* when they appear to be going in the wanted direction and *suppressed* otherwise. Such an opposite but synergic tendency in activation behaviour, again according our hypothesis, would be just possible thanks to some form of interglial communication through which the *stronger* pathways (the ones that are going in the wanted direction) order the *weaker* or *fruitless* pathways to suppress themselves so as to favour, in terms of global activation amount made available, what seems to be more useful in ongoing search. We have to remember that the work of search is developed in arousal

https://doi.org/10.46627/sipose.v6i1.409

activation (i.e. in a sub-threshold state) initially homogeneously distributed over the entire area affected by search and that, for this reason, no pathway can be advantaged by awareness. Hence, the supply in activation amount has to be guaranteed by some dynamics that also acts below the threshold of awareness. But in such a working condition, it seems to make sense to imagine that glia play a fundamental role, just by virtue of their properties of operating outside of awareness and of doing so much more freely and broadly than neurons can. Let us also remember once again, and let us so because it is a crucial concept, that there is voluntary search only if such a search, after being activated, proceeds in arousal activation conditions. If this were not the case, if the steps of search were immediately present in awareness, then we would be faced with something predetermined or a spontaneous association or even an intuition but not a voluntary search process.

To continue the discussion, we can observe that also in this search the request for an external isolation of WM seems to be essential, where WM is here constituted by the aware attention focused on the contents $Org_{(d)}$ and $Org'_{(non\text{-}d)}$ and the sub-threshold one covering STC*. The dynamics by which this isolation is set up is in fact the same as that hypothesized before and therefore also the inhibitory role of glia. The only difference is that, in this case, the thought process to be protected is well delimited by a beginning and an end with respect to which it is necessary to identify a *chain* of steps that unites them in a certain way, while in the pure voluntary thought process, the end of search is something that is found during the development of the process itself. Perhaps this basic difference could also influence the behaviour of glia both in their *constructive* and purely *protective* work. Anyway, coming back to the interrupted topic, we should point out that search for an AP* as anti-dystonic map to be followed for realizing a change in the organism-environment relationship is an extremely *pragmatic* thought process. Through that, a way to solve a problem whose solution can only come from outside (of thought) is essentially sought, not being in the position to count on the self-sufficiency of homeostasis or pure thought. For this reason, as said, overcoming a dystonia of this nature requires work in two phases:

I) search for a map in form of AP* and
II) physical implementation of the map i.e. of AP*.

In the second phase of this unitary procedure, awW takes on a different operational connotation. Search of an action strategy such as an AP* is a thought operation developed on mental contents representing possible empirical configurations of state. But, as is evident, the step following search, and the consequent choice of an AP*, is the execution of the chosen AP*. Now, in accordance with the characteristics of APs and the essence of awW presented in our perspective, once awW has chosen (said *yes*) something, it can only follow itself. That is, once awW has freely chosen an AP* as anti-dystonic map, it works, as far as it can, to create the physical conditions necessary to implement this map i.e. to translate the mental configurations forming the sequence AP* into environmental configurations of state. What does it mean? It means that awW has to execute all those defined steps which the sequence AP* requires. Each step, as repeated several times, consists of a well-determined operation that involves some change in the relationship between organism and environment. However, a modification of this kind can *only* be achieved through *movements* that, in our case, are defined by a pattern. Movement, understood in a broad sense, can be fundamentally of two types: a] *involuntary* movement, such as the *instinctive* or *reflex* movement or b] *voluntary* movement i.e. movement controlled by awW. As far as the first type is concerned, we are obviously not dealing with motor actions involved in an AP. Movements of second type, although they can be rigorously established in the various phases of their implementation – as in the case of what is foreseen in an AP –, can instead be performed only on the basis of procedures guided by awW. So, from this last specification we can conclude that awW, after having *mentally* chosen how to act, must now scrupulously put what it has decided into practice, that is, it must pass from the level of thought to that of the organic structures that make movement possible. In extreme terms, if we

pay attention, even movement can be reduced to a basic two-way procedure. In fact, performing a new movement consists in:

a) saying *no* to something – such as inertia, an ongoing motion, a spontaneous motion etc. – and
b) saying *yes* to another motor line

and all this right on the plane of the neuronal-muscular structures governing motor behaviour. We can hence conclude that, in the second phase of an anti-dystonic change based on an AP*, all awW has to do is mechanically apply and control what is necessary to physically actualize the action map previously developed in thought. With the possibility, as per properties of awW, to say *no* to the physical process in progress and to block the implementation of the map at any time and for any reason that is *felt* by awW as sufficient for justifying such program revision to itself.

Our overview of what is meant by *will* and *aware will* (aW) in an evolutionary framework has been given. We have seen how will, in the process of evolution, constitutes a leap in functional complexity, causing organism to gain a level of freedom from the contingency of its basic material dependence on environment never enjoyed before. Within this perspective, we have then construed the core of the present paper, that is, our hypothesis on the possible role of glia cells in dynamics just governed by will. Specifically, we have hypothesized a double role of glia in two voluntary key processes: the process by which a pure free thought is developed and the one that provides for a change in organism-environment relationship with anti-dystonic purposes. On both levels, we have therefor hypothesized that glia can be on the one hand directly active in realizing the processes themselves and on the other contribute to creating the best conditions for the work to be done.

Based on above, in the next section, we deal with the last matter that falls within our current interest. We want to extend the concept of *will* and hypothesize the existence of a second-level will that remains latent in ordinary existential contexts but that can be actualized if stimulated through specific and aimed *training paths.* We call this hypothetical second-level will, perhaps a little emphatically, by the name of *super-will* and, in line with the suggestion behind our proposal, we try to show that:

1) super-will still responds to an evolutionary logic based on the fundamental need for *coenaesthesia* that permeates the essence of any living organism;
2) the transition from ordinary will to super-will represents a further leap in the liberation of organism from its contingent relationship with environment and
3) glia could have a primary role in the processes regulated by super-will, maybe even more relevant than that one imagined in the sphere of ordinary will.

Of course, again, we cannot but adopt an absolutely hypothetical approach in dealing with this new and, in a certain sense, risky topic.

Super-Will Glial Memory and Freedom

By the term *super-will* (symbolically W^ from now on) we here designate a faculty of organism that can be considered as an extension of ordinary will, that is, will whose features relevant to our interest have been described in the previous section. Even this extension has to be framed within an evolutionary tendency that has as its guiding principle that one of pursuing coenaesthesia of organism considered in its own complexity that in turn has been also increasing in the course of evolution. By virtue of will and its indispensable functional correlates (i.e. memory and thought), organism has gained a considerable degree of freedom with respect to the pure mechanism of its primordial relationship with environment. Will expresses the possibility itself to choose among more different response options to be taken for overcoming a coenaesthesia problem that, as seen, is given by some dystonia occurring in the activation flux. But, in parallel to this *freedom*, will develops even the property to perceive types

of dystonia which the homeostatic (less evolved) system cannot detect or anyhow adequately manage. In particular thought, a source of anti-dystonic remedies with enormous potential, is in turn subjected to wholly inner forms of dystonia. It is precisely on the forms of dystonia of pure thought that will can act, identifying them and predisposing some specific intervention aimed at overcoming them.

This picture, that describes the ordinary condition of an evolved organism like a human being, is by itself enough to well represent what is meant by *freedom from environment in pursuing coenaesthesia*. However, beyond this reality, we can recognize glimpses that suggest the existence, precisely in the human organism, of a further virtual power to be exploited for obtaining a higher (and *uncommon*) level of emancipation from the bond with environment. Humans seem to be potentially able to overcome their own limitation, or what is usually considered like that, in sometimes truly surprising ways. In this context we no intention to focus attention on the several events that could confirm these considerations. Here we limit ourselves to examining a couple of interesting phenomena that strongly suggest the existence, at least in a virtual form, in human nature of faculties that, if well developed, could lead an individual to voluntary master his relationship with the rest of the world at a level of freedom that can well be defined *non-ordinary*. What we want to show is that a suitably *educated* organism, understood in its wholeness as psycho-physical entity – can lead itself to dominate, at least in some way, the external world and its stimuli, both in the sense of making the latter *superfluous* in causing sensorial experiences (differently from what occurs in ordinary conditions) and in the sense of drastically limit their effect on organism, once again moving away from normality. It has to be well emphasized that all this could translate into something real by virtue of a *strengthened* will that become *super-will*. Furthermore, our purpose is to hypothesize an intervention of glia, in this process of transition from will to super-will, that should be truly crucial, provided, of course, that our persuasion turns out to be not only theoretically plausible but also empirically founded. But before dealing specifically with the phenomena that we believe can derive from a super-will, we introduce an *ad hoc* hypothesis on glia and on their certain potential properties that, if well corroborated, would give just glia a leading role in genesis of the phenomena in question.

Glia Memory and Super-Inhibition

(*Faraday Cage*)

The key concept on which the hypothesis of a super-will (denoted by awW^ from now on), intended as further push towards an organic emancipation from environment and from dependence on external stimulations, precisely is that of *glia memory*. Let us hence see what the idea of the possible existence of such memory is based on, and then consider what results could derive from it once made active on a functional level (Bushong et al., 2002; Markham & Greenough, 2004; Bullock et al., 2005; Chadwick & Good, 2006; Ishibashi et al., 2006; Mesejo et al., 2015).

We begin our discussion by focusing attention on some morphologic-functional prerogatives of glia that come out to be already recognized in some way also on the experimental plane.

1) Glia, a type of astrocytes specifically, *structurally follow* the neuronal pathways → – i.e., as seen above, they give rise to joint neuronal-glial activation pathways →/⊃ – as they have the property of being activated in correspondence with synaptic activations.
2) Moreover, astrocytes have the ability to control synapses by carrying out diverse tasks including that of modulating synaptic transmission in both a strengthening and depressing way.
3) Glia communicate with each other by means of: i) an intraglial transmission system based on the internal release of Ca^{2+} ions and a gap-junctions delivery structure and ii) an

interglial system that uses substances such as neurotransmitters and others as basis of their communicational code, in this respect assimilating to neurons.

4) Glia, differently from neurons, can communicate, at an intraglial level, in both directions (⊃⊂), that is, they can cover the same transmission pathway without directional constraints.
5) In general, glia respond to neuronal activations e there are good reasons to suppose that they themselves have (or can have) some activating power towards neurons, presumably at the postsynaptic level by replacing the presynaptic neurons or agonizing with them.

Now, given these *didactic* premises as a framework for the matter, we can present the following crucial hypothesis.

We do not know exactly all the biochemical and anatomical-physiological details that characterize the process of withholding an experiential content and deposing it in that site of brain generically called *memory*. We know for sure that such process allows us to recall *backwards* what was originally stored in form of substitute imagine. However, both as regards perception (seeing, hearing etc.), both as regards physical sensations (pleasure, pain etc.) and – although with important distinctions – as regards emotions, the memory track, from which the memory experience is derived, does not reproduce the same perceptual or corporeal-sensory experience from which the track is formed. The imagine of an apple is not the same as the experience of an apple being seen or touched. Anyhow, if there had not been an apple seen or touched, there would not be any imagine of an apple that can be evoked at will. About this activity of memorization and recall to awareness of reproductions of original perceptual, sensorial and emotional experiences we can say that it is governed in its essence by neuronal processes that, in various ways, enable sufficiently evolved organisms not to lose their lived experiences in the flow of contingency. But, and this is the question, what can we say about glia that *faithfully* respond to neuronal activations thus forming the transmission pathways denoted by →/⊃? Namely, if neurons, thanks to their own excitatory dynamics, can give rise to strengthened circuits to the point of constituting a memory track of an experience, is it reasonable to hypothesize that glia associated in those circuits can operate in a similar way? Is it plausible to imagine that glia can also form some memory circuit parallel to the neuronal one? Can there be a glial circuit (at least on the virtual plane) that represents a copy of the track defined by the neuronal one and that is created according to a chemical-physiological *modus operandi* specific to glia? If this were the case then we would have something that can be schematized as follows:

neuronal track Tr→ of some "Ex" and
glial track Tr⊃ of the same "Ex"

both containing the original experience Ex encoded in different ways (Sul et al., 2004; Yu 2022; Curreli et al., 2022). Using a very simplified exemplary procedure, we can say that: if a neuronal pathway →, starting from a specific sensorial area where a percept P is formed, runs so as to reach other brain areas and there record the percept P (to be recalled later at will) in form of track Tr→, something similar could be done by glia associated step by step to the neuronal pathway taken into account so that a glial track Tr⊃ of P would be also created. In an architecture structured according to functionally associated neuronal-astroglial pathways, such as those formed by neurons and astrocytes, such a hypothesis seems not to be senseless. Once accepted, it is a question of ascertaining what all this can entail (Tognatta et al., 2020; Su et al., 2023). If we assume that – through the neuronal-glial, intraglial and interglial communication – a glial memory track Tr⊃ parallel to the neuronal memory track Tr→, what reverberations can we expect? To remember something, as just said, is to re-activate the memory track containing the image of that something experienced at the beginning of the entire memory process. Yet, if a sensation can become *memory* and thus broadly *image*, the latter cannot, at least through neuronal pathways, re-propose or re-generate a sensory experience. A sensory experience is

generated by environmental stimuli and a memory image cannot, just because of the neuronal structure and physiology themselves, functionally replace an external stimulus. But now let us consider the property of glia mentioned in the point 4 of the list exposed above. Glia enjoy the prerogative of being able to convey information in both directions, unlike neurons that rely on unidirectional intracellular electric transmission. Thus, if we put together the hypothesis about the existence of a glial memory track parallel to the neural ones with the structural capacity of glia to send messages in one sense as in its opposite, we can conjecture that glia has the at least potential power to transmit the content of a given track Tr⊃ – originally formed together with the correspondent track Tr→ – from the memory areas to the portion of sensory area where such content finds its *archetypal root*. If this conjecture is realistic, in merely theoretical terms, at least a further basic question arises.

> If it is plausible to suppose that a track Tr⊃ is *backwards transmittable* by following step by step, stage by stage, the pathways →/⊃ opened in the beginning, how can such a potential be actualized? This is to say: under what conditions could a track Tr→/Tr⊃ activated as image reach the corresponding sensory area and *topically* stimulate it, without the intervention of external stimuli, so as to generate a bodily sensation in all its consciousness potency?

The fact that glia are able to produce and locally secrete neurotransmitters is something already verified. For this reason we cannot exclude that a glial pathway has the power to distally affect clusters of neurons and activate them by releasing specific neurotransmitters. If this is true, glia involved in the process could use precisely the same neurotransmitters used as synaptic mediators to trigger the primary dynamics of perception-memorization of the experiential content of which glia conserve just memory. In any case, once assumed this challenging theoretical framework, the issue that arise is obviously to investigate what specific and contextual features have to affect an organism in which such a phenomenon occurs. In other word, if we admit the existence of a sort of potential *glia memory*, the next step cannot but be to identify the neuronal-glial state in which organism should be in order to obtain from glia not a memory in form of an image but a real, wanted and targeted *hallucinatory* experience, of whatever sensorial nature it is.

Glia Memory: Possible Experimental Directions

It has also to be said that the hypothesis about the existence of a glia memory, beyond its theoretical plausibility, should be empirically tested, in the sense that it should be ascertained on an experimental plane whether an organism immersed in a state of adequate *isolation* from environment and from any potentially disturbing stimulation gives glia the necessary conditions for:

a) triggering a backwards transmission and
b) making effective their power to autonomously and directly activate precise target sensory areas (Parri et al., 2001; Nett et al., 2002; Aguado et al., 2002; Hirase et al., 2004).

The idea, as said, is based on the supposition that a *trained* will comes to favour the emergence of physical and mental phenomena which an organism ordinarily keeps in a purely virtual dimension. If therefore, similarly to what occurs in the neuronal memory mechanisms, certain *facilitated* pathways are defined in such a way to create an *indelible mark* of the original experience in the neuronal-glial tissue, it would be interesting to answer at least three important questions that exactly arise from the persuasion that a *latent super-will* exists in each human organism.

I) Can determinate conditions of profound psychophysical isolation, with attention *super-focused* on the memory image Ex′ that awW^ (i.e. super-will) intends *perceptually* to revive, determine a *super-activation* of the glial track Tr⊃ containing Ex′ – activated by the voluntary act of evocation together with the corresponding neuronal track Tr→ of Ex′ – that

in turn generates an impulse to a backwards transmission of the imaginative content Ex'? Symbolically:

sensory area A →/⊃ Tr→/Tr⊃
super-activation Tr⊃ ⊃ sensory area A

II) Does the backwards pathway faithfully follow the original one? Namely: is a super-activation of Tr⊃ in memory area sufficient to impart the wanted structural routing to the content Ex' of Tr⊃ with absolute accuracy? Is such an ongoing state enough to force the image Ex' within the marked pathway and finally lead it to precisely touch each item of area A from whose perceptual product it has been derived?
III) Once reached target A with due precision, does glia have the effective power to promote the activation of those neurons that, if activated, would offer in feedback the desired percept thus closing the cycle of the activation senses?

So, given the super-isolation conditions ensured by super-will – a topic we will talk about shortly –, the issues just raised in the three previous questions could be experimentally detected by trying to ascertain:

a) whether there is some correspondence between the super-activation of the brain areas supporting the evoked image of the percept and an equally marked activation of the well-circumscribed sensory area from which the perceptive experience should arise;
b) whether the super-activation of the memory areas is followed by an activation of specific glial pathways aiming at some exact target sensory area;
c) whether these super-activated glial pathways, once reached their target, are effectively able to *topically* (point by point) activate those portions of sensory area whose perceptive result is the model of the memory image now restored to the original;
d) whether, to conclude, the *upstream* (in memory areas) super-activation of an image effectively causes an immediate super-activation of well-determined glial pathways and whether this aimed super-activation is such as to make glia able of exerting an autonomous activation action on precise blocks of neurons *downstream*.

All this in order to better understand whether a super-activation produced in conditions of super-isolation really allows glia to make that significant leap in functional power that would also represent a relevant fact from an evolutionary viewpoint.

Super-Inhibition (Faraday Cage)

If glia memory exists and if it can physically support non-ordinary processes, it is also imaginable that such property needs some contextual help to become effective. This is to say that, in such a perspective, awW^ has the task of creating the organic conditions so that glia, over time and with perseverance, *learns* to carry out functions which their non-ordinary role claims. We have said that awW^, in analogy with awW, predisposes the isolation of the brain areas in which a specific activity is occurring, i.e. the brain areas globally defined here as *working memory* (WM). On this level of volition, we can suppose that the request for isolation is even more pressing and that the required *super-isolation* in its turn needs to be appropriately promoted. In this respect, we hypothesize that awW^ works for *instructing* both neurons and glia to isolate what is of interest as much as possible and in the most delimited possible (Houdes et al., 2008; Mesejo et al., 2015; De Pittà & Brunel, 2016; Sajedinia & Hélie, 2018; Dzyubenko et al., 2021). The contribution required to glia, just by virtue of their property to act ubiquitously and without particular structural transmission constraints, is similar to the one already seen regarding awW. However, on this plane of intervention, there would be a demand for supplementary and more intense task for which glia themselves would have to be educated

through practice. Such issues could be experimentally dealt with *diachronically* by trying, for example, to verify whether:

> through a suitable training, the capacity of inhibitory glia is strengthened both in intensive – trend to increase the inflow of intraglial Ca^{2+} in specific regions of the nervous system with empowered propensity to trigger aimed inhibitory mechanisms etc. – and spatial – recruitment of more glia by other already enough trained glia to widen the surface of inhibitory action etc. – terms.

Yet even a *synchronic* approach to this matter would be helpful. For instance, taking individuals well-trained in these practices as the object of investigation, the glial (but also neuronal) processes underlying the phenomenon of super-inhibition could be temporally and topically followed while they are performing their task by a super-voluntary request. Thus, to conclude, if we assume that super-will exists and that it can favour the emergence of certain non-ordinary events only by isolating the focus of its purpose from everything else in an absolute way, then we have also to account for how this sort of *Faraday cage* can develop to exactly act as an incubator during the gestation of those events.

In the next and last section, we will try to expose in a scanned way some phenomena that we hypothesize can arise from this expanded vision of will. We will try to do it by focusing our attention just on role of glia both in directly determining such phenomena and in creating the necessary conditions for their occurrence. From the general framework of what will be hypothesized it should emerge that super-will, as well as it is conceived here, is a non-ordinary faculty, by this meaning that it constitutes a centre of power that places those who cultivate it assiduously at a level of psycho-organic potential that can rightly be defined as *super-normal*. A super-normality that, on the other hand, represents a further push towards the emancipation of organism from environment, a push so strong as to lead organism, within certain limits of course, to *do without* external stimuli and to *dominate* their effects with a mastery not ordinarily found.

Some Phenomena of Super-Will

From what has been exposed it emerges that awW^ is a form of evolution of ordinary will awW considered previously. It constitutes, if we may say so, an *impetus* not only to go beyond the immediate contingency, in which the organism-environment relationship is constrained, but also to become somehow independent from this relationship itself. Effectively controlling the reverberations of the external stimuli on organism and even substituting the stimuli themselves through sensorial self-productions represent precisely the perspective which awW^ sets as its own goal. We can say that if ordinary will awW begins by a *yes* or *no* to a specific *status quo*, awW^ comes into play by a radical *no* and, from here, reshapes its own reality. In these pages we consider only some processes that could be framed within this inspiration of super-volition. A couple of a constructive nature and a couple with inhibitory purposes.

Firstly, we try to outline how awW^ could arrange psycho-physical mechanisms to produce on its own what is necessary for receiving feedback experiences that would otherwise be completely dependent on the intervention of external factors. This, under the hypothesis that glia play a decisive role in achieving the objective.

Hallucinated Perceptual Experiences

The hypothesis underlying the possibility to create perceptual hallucinations (and even physical sensations such as pleasure or pain), thanks to some properties of glia – sufficiently educated by an aimed practice –, is a hypothesis that can arise not only from the peculiar nature of glia but also from some considerations that can be made on the hallucinatory (morbid or induced) phenomena as themselves. Indeed, if we observe the essence of a perceptual hallucination (for instance induced by psychoactive substances such as the LSD) we can notice that it is always given by an experiential content that recalls, in a

more or less faithful way, perceptual experiences actually had in the past. Even the most *warped* of the hallucinatory contents or the most *bizarre* composition of details can anyhow be traced back to perceptive experiences ordinarily formed by means of sensorial channels starting from external stimuli. Thus, in a hallucinatory experience where certain sensorial areas are just active without any external stimulation, it really seems that memory, as the store of the tracks of past perceptual experiences, somehow intervenes in the process and that it intervenes in a fundamental way. The spontaneity of a hallucination – as in the case of morbid manifestations – or the induction to it by hallucinogenic substances turn out to be processes in which material is being retrieved from something that already physically exits in the organic system, i.e. in its memory. If this is at least plausible, it would be interesting to understand how memory can *actively* take part in determining such non-ordinary phenomena. We now proceed by presenting our conjecture and we do it using again a schematic exposition with the aim of highlighting what role glia should have in each phase of the hallucinatory process voluntarily arranged.

A *deliberate* hallucination prepared by awW^ would have to develop, based on our conjecture, according to the stages summarized and schematized as follows.

a) awW^ fixes as its own WM, i.e. as total area on which attention is focused:
   1) the memory areas, where the aware attention is focused on a particular double track Tr→/Tr⊃ supporting some memory image I and
   2) the sensory area, where the sub-threshold attention is focused and where the percept P corresponding to the memory image I should be effectively re-evoked.

b) Given the premises defining the areas of WM, the most important and, doubtless, theoretically riskiest phase of the hypothesized process should start. In a state of attention hyper-focused on the image I that is wanted to be converted into the hallucinated percept P, it has to be made sure that the glial memory track Tr⊃ (associated to the neural one Tr→) is super-activated, namely that it reaches an activation level being non-ordinary.

c) For this to occur, still hypothetically, it is necessary that awW^ arranges a real super-isolation around the areas covered by WM – i.e. around the double track Tr→/Tr⊃ and the specific sensory area being the target of the hypothesized backwards journey of glia. Such *Faraday cage*, as we have metaphorically called the condition of super-isolation, turns out to be of crucial importance for causing the emersion of the glial track Tr⊃ and triggering the transmission of the content I from the memory areas towards the sensory area that potentially contains P of which I is just the memory. Symbolically:

   Tr⊃ I ⊃ … ⊃ I – (∷ P) SA

   It is highly plausible that, in a vision like this, *support glia*, i.e. glia that should ensure the state of marked and aimed isolation – as well as neurons taking part to the operation – have to be somehow trained in order they can acquire a sufficient strength and ability for performing their task. This is to say that awW^ must persevere in requiring glia and neurons to accomplish their non-ordinary effort, itself pouring out a commitment to massive and localized concentration. Only in this way, only thanks to a Faraday cage well-built around the entire region of WM (memory area, glial pathways and target sensory area) the hypothesized conditions for starting and finishing the backwards memory-sensitivity process can be guaranteed.

d) If the super-isolation around the region of AW (specifically around the track Tr⊃ of I and the glial memory pathways starting from Tr⊃ and aiming at the target sensory area containing the matrix of P) is well-realized, the hypothesized backwards journey of memory glia should arise. Furthermore, what is essential, this journey must develop in such a way as to topically re-design (just backwards!) the original journey from sensory

area in which P has taken shape towards memory areas where Tr⊃ has been defined – a bit as if, from a painting, the artist's gestures in act of creating the work were retraced backwards. Therefore, if Tr⊃ is originate from the journey:

$$\text{Stimuli} \rightarrow \text{Sens-Areas}_{\text{n-pathways}} \rightarrow/\supset .. \text{Inter-Areas}_{\text{m-pathways}} \rightarrow/\supset .. \text{Tr}\supset$$

(schematizing the journey at the extreme, of course),
the backwards journey should be:

$$\text{Tr}\supset_{\text{m-pathways}} \supset .. \text{Inter-Areas}_{\text{n-pathways}} \supset .. \text{Sens-Areas},$$

so that the copy in form of an image imprinted in the track returns step by step to its *archetypical model*, retracing its genesis in all the procedural complexity that has characterized it.

e) Pushing our hypothesis to the limit – i.e. admitting that memory glia are capable of transporting the image I of Tr⊃ up to the target sensory area – we also hypothesize that, in a state of perfect isolation, the terminal activation of memory glia can be followed by the localized activation of neurons that, becoming excited as if in correspondence with a specific external stimulation, give the percept P (original model of I) as feedback through the ordinary pathways that bring sensorial contents to awareness.

Now, this hypothetical process, we must repeat it, seems to be theoretically plausible, as it does not conflict with the morphologic-functional properties of glia that have been ascertained so far. On the other hand, it is obvious that each step of our scheme should be experimentally inquired, as already mentioned. For instance, taking individuals well-trained in certain meditative practices or experts in self-hypnosis techniques as experimental subjects, it could be investigated whether the various phases and the various inhibitory and activating contributions, as well as they are marked in this schematic exposition, are also confirmed in the neuronal-glial system of a subject while the process is in progress. Also, regarding the concept of *strengthening exercise* on the ability to produce a voluntary super-isolation around the WM areas, it would be extremely important to establish whether such a *knowhow* is empowered over time precisely in terms of and thanks to those specific intra-and-interglial communication mechanisms that have been imagined here.

In conclusion, what has been exposed in a purely theoretical dimension suggests the advisability of promoting empirical investigations and phenomenological analyses to answer some relevant questions such as whether:

1) it organically occurs that a localized activation of glia arises in correspondence of a determinate memory track;
2) such an activation propagates backwards aiming at sensory areas and following a rigorously defined pathways;
3) once reached the target, the glial activation effectively causes an autonomous neuronal excitation in well-circumscribed items of the target sensory area (and not elsewhere), giving rise to the formation of a percept without any intervention of external stimuli;
4) this work turns out to be possible only thanks to a super-isolation (Faraday cage) around WM determined just by awW^ by virtue of its acquired power of imaginative concentration and
5) the efficiency of super-isolation is truly strengthened by the practice imposed by awW^.

Obviously, for each question raised just now, it should be highlighted how, in the glial communication code, all this information necessary to coordinate the ongoing process is formulated, conveyed and received by the structures variously affected.

Leaving the hallucinated perceptions aside, we can move on to consider another interesting phenomenon whose paternity is attributable to an intervention of awW^. To do it, we enter the sphere of emotional processes.

Hallucinated Emotions

The potential of a strong awW^ is not limited to the ability to produce perceptions as a generative replacement for environmental stimuli. Even an emotional experience can be somehow *hallucinated*, in the sense that it can be extracted from any eliciting situational context and experienced in its phenomenal manifestation. Hallucinating an emotion does not mean simply to evoke it by remembering some emotionally charged autobiographical episode. If we accept a somewhat sophisticated description, we can say that the voluntary hallucination of an emotion is a path tending to grasp emotion as a pure experience, free from any environmental or internal event related to it as a trigger. However, differently from hallucinated perceptions and physical sensations, an emotion does not find a clear boundary between memory track of the emotion and the emotional experience itself. The recall of an emotion directly affects the organic areas that generate the corresponding emotional state. Therefore, hallucinating an emotion has to be intended as a process qualitatively separate from that one by which a voluntary hallucinatory perception arises, where the memory image of an original perceptive experience is something substantially different from the sensorial experience as such. So, let us see how the wanted hallucination of an emotion can be conjectured in harmony with what has just been said about the features which such a non-ordinary experience should possess. The goal, according to our view, is to reach an emotion and experience it as something independent of everything else, in its phenomenal essence. To achieve such a experiential state, a three-phases process can be hypothesized.

I) awW^ evokes a particular emotion E by using ordinary means such as emotionally significant events of the individual's life or – as well as it is practiced in certain meditative techniques – by exploiting *support objects* with specific properties to induce determinate emotional states. Once obtained the wanted emotional state E, awW^ fixes awareness exactly and intensively on E.

II) At this point, the procedure is to completely super-isolate E, and to do so also with respect to the recalled autobiographical context or the support object by means of which it has been elicited. The Faraday cage must isolate only E.

III) Once E has been super-isolated in its purity, the process can go on by *super-agonizing* (i.e. increasing the amount of activation) just on the emotional areas whose affection physically leads to the onset of those qualities of E that are subjectively experienced so as to give them maximum intensity.

Even as regards this sphere of possible action of awW^, it should be empirically verified:

1) whether there are in fact organic indicators of a super-isolation that protects the physical structures from which E emerges;
2) how this Faraday cage comes to be realized, with particular regard reserved to the role played by glia in such realization – i.e. it should be investigated what occurs in locally inhibitory terms, with respect to very defined portions of emotional areas, as well as we have already specified it should be done to understand the mechanism of isolation and super-isolation in general terms and, finally
3) whether the condition of super-isolation around E achieved in this way is accompanied by a synergic neuronal-glial hyper-activation on E that maximizes the presence of this emotional state in awareness:

$$\rightarrow / \supset^{\text{hyper-activ}} (::E) \text{ Emot-Areas.}$$

We can conclude that, in this operation of emotional hallucination, glia would have the task of: i) offering its super-isolating contribution in building the Faraday cage around E – only around E and giving up any memory or contingent association – and ii) working in synergy with neurons in order to convey greater amounts of activation on the emotional areas supporting E.

https://doi.org/10.46627/sipose.v6i1.409

Returning to the general topic, we can state that, in accordance with the hypothesis put forward, a well-trained will (such to become a super-will awW^) can improve and strengthen the neuronal-glial relationship to the point of giving this relationship the synergic ability to produce phenomena that are ordinarily not reachable. Phenomena that, as seen, have the characteristic to constitute aware experiences produced inside organism itself without they originating from external stimuli, as ordinarily occurs. Anyhow, it can be also conceived that awW^, in addition to this *constructive* power, possesses also one that can be defined as *super-control* over emotional and bodily states that, being unwanted, demand to be eliminated (or at least modulated) in a condition of self-sufficiency. Let us now see what this means by taking into account how awW^ can control and, in principle, even eradicate specific undesired emotions.

Super-Control and Emotional Inhibition

Under the general defining label *Emotional Inhibition* we can bring three distinct processes having three different goals.

1) The modulation of an unwelcome or abnormal emotion (such as a paralyzing fear) in temporally contextualized terms.
2) The extinction of a rooted emotional state that can be consciously referred to some past autobiographic event that generated it.
3) The extinction of a rooted emotional state with respect to which the original autobiographic experience of its causation has been removed.

Let us consider the first dynamics.

Contextualized Modulation of an Emotion

The need to give up an unwanted emotion, or one that negatively conditions the implementation of a desired action, can induce a well-trained will to activate some dynamics having an efficacious inhibitory effect on the ongoing emotional manifestation. In order to best face a situation like this, we hypothesize that awW^ can adopt a procedure initially similar to the one described just above regarding the hallucination of an emotion. It is thus imaginable that awW^ super-focuses its attention exactly on the emotion E which it intends to repress. Even in this case, the area of WM is given by the portion of emotional areas from which E arises. Furthermore, even in this case the action field of the Faraday cage – the super-isolation – should be strongly centred on E. The difference, with respect to the hallucinatory process, is that the last phase of the work of awW^ should be to promote a deep super-inhibitory action on E – by using neuron-glial channels in a synergic way with this aim – rather than increasing the activation of the latter as it has been supposed about the hallucinatory practice. It is absolutely evident that all considerations made previously regarding super-isolation and targeted super-inhibition again apply here. Also including the various suggestions on possible empirical investigations to be carried out Delgado & Navarrete (2023).

Extinction of a Rooted Emotional State with Autobiographic Origin Being Aware

Often an emotional perturbation, that negatively conditions the psycho-physical well-being of an individual, originates from traumatic episodes that mark the biography of that individual, forcing him to suffer their reverberations over time. In similar circumstances an original association between an episode with a strong emotional impact and the emotion itself E that derives from it. Then, the association between the event – or rather a track of it – and the emotion E can be stored in the memory areas so as to remain evocable as such, i.e. as a precise association, according to the will of the subject or even spontaneously. Now, remembering an emotion is in itself equivalent to reliving the emotion – although not necessarily with the same intensity – and hence in fact, in the context taken into consideration, we can describe the onset of a persistent emotional nucleus as follows:

I) at the time t_0 an event Ev (perceived through senses) causes an emotion E in such a way to form the association Ev ─ E;
II) if the emotional impact of the experiences is particularly intense (or traumatic) then the dyad Ev' ─ E can be condensed into an associative memory track;
III) the association formed between Ev' and E can be evoked at any time t_x after t_0 in such a way the memory Ev' of the event Ev causes the emotion E resurface.

Based on this generative process, intervening to eradicate an emotional nucleus, rooted in the memory-emotional associative area, means acting according to a criterion of selective inhibition tending exclusively to break the association Ev' ─ E that refers to the episode Ev originally triggering E (Han et al., 2012). How? In line with our hypothetical system, the guiding principle of this dynamics could be succinctly outlined as follows:

on the one hand, *super-isolate* the track Ev' in memory areas and, on the other, *super-isolate* the emotion E in the areas of emotional genesis

(in accordance with the logic of the super-isolation of the areas covered by WM already discussed). Within a Faraday cage prepared in this way, there should be the conditions to perform a deep and targeted inhibitory action on the associative pathway Ev' ─ E that, if insisted in intensity and/or over time, can lead to the extinction of the pathway itself, as well as it is wanted.

As it is easy to notice, this is a process that broadly resembles the *cathartic-therapeutic* technique of fully reliving a traumatic experience – in a state of physical safety – in order to eliminate its emotionally painful and enduring aftermaths. Anyhow, again, the reference to the advisability of experimental verifications about the matter is due. In this case, it should be specifically checked whether a super-isolation fixed on Ev' and E is such as to allow the triggering of an inhibitory action purposed exactly to extinguish the associative relation existing between them.

Extinction of a Rooted Emotional State with Autobiographic Origin Being not Aware

We can say that a condition of rooted emotional perturbation, the autobiographic origin of which is not present at the subject's consciousness, is a classic case theoretically and clinically pertaining to psychoanalysis. Here however we deal with the topic in different terms and perfectly framing it in our hypothetical context in which awW^ is placed. In order to fully understand what is mean by *extinction of an enduring emotional state whose origin is consciously unknown to the subject* we first present, again in a schematic way, the prototypical mechanism by which such a state imposes itself.

Well, an emotion E, that subsequently establishes itself in the structure of organism as a constant and unwanted presence, mostly arises from some traumatic event or one that anyway has a strong emotional impact. Therefore, we can schematically represents this situation as:

Stimuli ─> (::Ev) Sens-Areas →/⊃ (::E) Emot-Areas

i.e. we have the perception of the event Ev that causes a vigorous reaction in the emotional areas that is in turn felt in consciousness as an acute and strongly painful emotion E. As said, an event like this is then registered in the memory areas as an association Ev', E between the track of the original Ev and E itself. But, unlike the previous case, we have here that – for some *unconscious* reason, the memory Ev' of Ev is *removed* from the space of the aware autobiographic events, thus leaving the subject orphaned of the original reference to which E and its burden of pain can be linked. In cases like these, that are very frequent in truth, a strengthened will such as awW^ could intervene by making use of glial memory, the existence of which is assumed, that originally allowed the formation of the associative bond Ev', E and that, unlike neuronal memory, is hypothesized as not subject to the process of removal. So, according to this supposition, awW^ should promote, again thanks to the support of a Faraday cage construed

around the areas affected by the operation – a sort of re-enactment of the original experiential dynamics by just following the backward glial journey. That is, awW^ should:

1. super-isolate the emotion E in the emotional areas so as to intensify the presence of such condition in awareness;
2. thus activate the glial pathways E ⊃ Ev′ (backwards) that lead from the emotion E to the memory track Ev′ the association of which with E has been removed in the neural pathways;
3. finally allowing the glial pathways, once reached the track Ev′, of re-activating it through an autonomous stimulation exerted on neurons.

Super-isolation in this process should affect:

1) the emotional areas – and precisely the organic structures supporting E – so as to control any other solicitation that could compete with E for access to awareness and
2) the autobiographic memory areas, just allowing the glial pathways E ⊃ Ev′ to become active and reach their destination – the track Ev′ – according to the hypothesized properties of the glial system of developing memory contents and recovering them by backward activations.

This is a process that, if performed in the conjectured terms, could consciously restore the image of the primordial trauma in its memory-emotional entirety. Afterwards, on the basis of this re-established association, awW^ can proceed with its work of extinction in the same way described above concerning the elimination of a deep-rooted emotional state whose episodic origin is present in the subject's awareness.

CONCLUSION

Even at the end of our overall hypothesis, it seems not to be superfluous to reiterate the belief that every step theoretically conceived here should be subjected to careful phenomenal investigations, possibly in experimental settings too. In these pages, as a complement to the conjectures put forward in the course of our discussion, we have tried to provide at least some indication about the directions to follow for designing and carrying out the hoped empirical evaluations, with specific respect to the key issues that could confirm the correspondence between the theory and the organic phenomena observed in their actuality or deny any factual sustainability of the arguments. Furthermore, we have to specify that our purpose is certainly not to propose a "method" to overcome psycho-emotional conditions that can sometimes be extremely serious. On this matter, as well as on the others considered in this paper, we want only to schematically and essentially outline what we hypothesize could fall within the potential of will and a suitably trained super-will as we have imagined them. Returning to the basic idea on which our entire vision is founded, we can conclude that:

> if the primary goal of organism is to pursue its own well-being (its own coenaesthesia) and if will and super-will, as *superior* expressions of organism, respond to this fundamental need – moreover in a perspective of emancipation of organism from material contingency –, then it seems to be consistent to think that such higher faculties, using their power to influence the neuronal-glial structures as imagined, can have a positive and decisive impact in preparing the conditions for the well-being of organism to be achieved. All this, both by providing something that is missing and by eliminating what is unwanted. At least, within certain limits.

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