The Role of Sentience in the Theory of Consciousness and Medical Practice

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Abstract: In this target paper, I focus on the concept of sentience in relation to the theory of consciousness and to practice in the medical sciences, neurology and psychiatry, regarding both diagnostics and therapy. Following authors in this field, I distinguish two modalities of consciousness: sentience, in the sense of being awake and capable of feeling (e.g., basic sensations of hunger and thirst, pain) and, second, cognitive consciousness, in the sense of thinking and elaborating on linguistic and imagery representations. The physiological correlates of sentience are proposed to be the systems underpinning the dynamic control of biochemical homeostasis, while the correlates of cognitive consciousness are considered to be patterns of bioelectrical activity in neural networks. I claim that sentience needs to be taken in account, if better tools are to be developed for medical diagnostics (e.g., by identifying biochemical markers) and therapy (e.g., using new pharmacological drugs and brain stimulation technologies targeting the correlates of sentience). The main hypothesis presented here to support this claim is that cognitive consciousness depends on sentience, but not vice-versa, implying that medical practice should also address the physiological correlates of sentience in the diagnostics and therapy of disorders of consciousness.

Key Words: Sentience, Consciousness, Glial Cells, Neurology, Psychiatry, Homeostasis, Allostasis.

Introduction

Theories of consciousness have attracted widespread interdisciplinary attention, aimed at delivering developments and practical applications in several fields, including neurological rehabilitation, mental disorders therapy, decision-making in economics, and artificial intelligence. A recent manifesto signed by 58 researchers (Michel et al., 2019) reviewed challenges for the application of theories of consciousness to the medical area, where new therapies - such as transcranial Direct Current Stimulation (tDCS) - have presented positive results which existing theories cannot fully explain. The authors call for "the recognition of consciousness science as an indispensable area of biomedical research…Achieving a better understanding of consciousness is critical to multiple medical, scientific, legal, and ethical issues, such as the detection of consciousness in anesthetized or non-communicating patients, infants, other animals, and machines; epilepsy seizure classification; the measurement of well-being and happiness; and the assessment of moral responsibility" (Michel et al., 2019, p. 1).

In the same direction, Adrian Owen, one of the pioneers in researching Prolonged Disorders of Consciousness, asked in a recent conference in this area: "What does it mean to be awake, but entirely unable to respond, and what can this tell us about consciousness itself?" (Owen, 2019, p. 6). He reported the use of imaging technologies "to detect covert conscious awareness in patients who are behaviourally entirely non-responsive (e.g., vegetative, comatose) and even to allow some of these individuals to communicate their wishes and thoughts" (Owen, 2019, p. 6).

Owen´s focus, in his outstanding medical work, was on 'higher level' cognitive consciousness (e.g., higher functions involving symbolic language) but - here I claim - the understanding of the 'lower level' processing underpinning sentience (as, for example, the susceptibility to feeling pain in the presence of noxious stimulation) could be equally useful for medical diagnosis and therapy. The existence of 'two awareness networks', one related to arousal and glucose metabolism, and the other to cognitive representations of the environment, was mentioned by Laureys (2019) in the same conference. Seth (2019) expanded the conceptualization of consciousness to require three categories: *Level* (corresponding to arousal), *Content* (corresponding to cognitive representation), and *Self* (a third category, about the person being interoceptively aware of herself).

In this paper, I focus on the conceptual relation of sentience and cognitive consciousness, arguing for their different physiological correlates and the relevance of considering sentience in medical practice. The main hypothesis is that cognitive consciousness *depends on sentience*, implying that more attention should be given to the neural correlates of sentience in medical diagnostics and therapy. The minimal requirement for considering a person minimally conscious is, according to this line of reasoning, if she *can feel* basic sensations such as hunger, thirst and pain. The capacity of feeling is here conceived as closely related to the capacity of dynamically controlling the physiological processes of homeostasis.

Higher-level capacities related to connectivity patterns of bioelectrical neuronal activity in the neocortex, such as verbal or imagery thinking, the retrieval of episodic memories and action planning (e.g., imagining playing tennis, a technique for assessing residual consciousness in vegetative states; Owen et al., 2006), may not be adequate *as a general standard* for medical diagnosis of prolonged disorders of consciousness, since – according to the proposed reasoning – in many cases the person may not be able to perform these tasks but still be able to consciously experiencing basic sensations. Taking general anesthesia as an example, if the main criterion is not being able to feel pain, the goal of the procedure would be broader than the loss of cognitive consciousness. In some cases, the neural correlates of cognitive representations may not be the main target of treatment, since they correspond to a high-level specific ability that is not necessary for lower level sentient experiences, which also deserve attention for proper medical and also bioethical reasons.

Conceptual Issues

The concepts of sentience and cognitive consciousness, as well as related concepts, such as *affect*, *feeling* and *qualia*, have been approached historically in several different ways, resulting in their semantic ambiguity. Before embarking on the translational endeavour of relating these concepts to medical procedures, some clarifications and elaborations on how the concepts are used here is needed.

According to the Merriam Webster Dictionary, the term *sentience* refers to “feeling or sensation as distinguished from perception and thought” (https://www.merriam-webster.com/dictionary/sentience). This concept of sentience can be understood as *potential* consciousness: the *capacity* to feel (proprioceptive and exteroceptive sensations, emotional feelings) and to have qualitative experiences, while cognitive consciousness refers to the actual experience of thinking with mental representations. This concept of ‘cognitive consciousness’ stems from Baars (1988, republished in Baars, 2019) and relates to ‘resonating’ neocortical activations in the *Dynamical Global Workspace* that processes conscious information.

In affective neuroscience, *sentience* refers to the *affective drive* that *makes* us conscious. Conscious affective experiences as pre-reflexive or vague sensations and emotions are classified as ‘anoetic consciousness’ (see discussion in Almada et al., 2013; Panksepp, 2005; 2010; Vandekerckhove and Panksepp, 2009), while *cognitive consciousness* is conceived within the ‘noetic’ and ‘self-noetic’ types of consciousness (‘self-noetic’ when the object of knowledge is the conscious system itself). Sentience can also be conceived as co-extensive to the (Freudian) ‘unconscious’, and similar to a family of concepts mentioned by consciousness theorists, such as Primary Consciousness (Edelman, 2004) or the ‘pre-conscious’ domain referred to by Velmans (2002) and Dehaene et al. (2006).

The term ‘sentience’ has been mostly used in studies about *animal* consciousness. *Animal sentience* has been defined as “the *minimal capacity* (italics by APJ) to have subjective experience of the qualities associated with external and internal sensations, as well as affective and motivational states for phenomenal consciousness” (Allen and Trestman, 2016). According to this definition, sentience is not identified with full conscious activity, but with a “minimal capacity” that is manifested in different forms and to different degrees in different biological species, including ourselves.

The usage of a variety of concepts about sentience begins in Spinoza’s *Ethics* and remains in the contemporary approaches of Panksepp (1998) and Damásio (1999). According to Spinoza, “Between appetite and desire there is no difference, except that desire is generally related to men insofar as they are conscious of the appetite. So desire can be defined as appetite together with consciousness of the appetite” (Spinoza, Ethics, III Proposition 9, Scholium). In this approach, not only the appetite but all types of ‘striving’ (Le Buffe, 2015) are related to a general condition, the *conatus*, that corresponds to the affective drive belonging to the domain of sentience. In the above quotation, the ‘desire’ is an actual conscious experience (an emotional state directed to an object of thought) in which the appetite is expressed. For instance, hunger is a type of ‘appetite’, while the ‘desire’ of eating, e.g. bread with cheese and ham, is the conscious expression of the ‘appetite’ directed to a cognitive object of thought (the sandwich).

Following Spinoza’s distinction, I use *sentience* to refer to the *capacity of feeling*, a *dispositional state* that contains a range of potentialities, of which only a subset is made actual at each moment in the consciousness of a person, depending on her interaction with the physical and social environment. Where and when there is attunement of the internal disposition with the external affordance, then a specific conscious cognitive or emotional content is determined; in other words, the cognitive or emotional content is not determined by the affective drive alone. This distinction is important for scientific approaches, because scientists can measure physiological dynamic patterns underpinning the sentient capacity but cannot measure conscious experience (including the qualitative states – *qualia* - attached to mental representations). Information about first-person conscious experiences depends on verbal or non-verbal reports by the conscious subjects, to be interpreted by the scientist, on the basis of her first-person perspective. Therefore, the study of sentience is within the 'Easy Problems' conceived by Chalmers (1995), while explaining full consciousness is the 'Hard Problem'.

In Phenomenology, sentience implies only the existence of a '*here-and-nowness*' (the term 'nowness' was used by Nunn, 2016) or a *presence* (Seth et al., 2012) that *is able to feel*, but *without* the structured experiences that we find in full conscious episodes. In Neuroscience, 'feeling' (in the sense of the term 'sentience', as used here) was recently the object of a multi-author review, in which they added the qualification 'physiological' (Pace-Shott et al., 2019). *Physiological feeling* processes refer to the *physiological correlates of the sentience capacity* - such as the interoceptive loops between the central nervous system and the whole body interacting with the environment – that *result* in conscious cognitive and emotional contents. The authors arrived at the conclusion: "changes toward and away from homeostasis, not only within the autonomic nervous system but in all systems of the body (e.g., metabolic, cardiovascular, immune), contribute interoceptive information to the CNS. The integrated output of multiple physiological systems may provide highly complex inputs to central mechanisms that *produce* (italics by APJ) the conscious experience of feelings, moods and emotions" (Pace-Shott et al., 2019, p. 294). In regard to my previous example of eating bread with cheese and ham, 'physiological feelings' correspond to the affective drive (the 'appetite' to eat) while 'conscious experience' corresponds to the actual conscious experience; in the previous example, eating the sandwich (with pleasure, by carnivorous persons, while for vegans the ham is disgusting).

It is also important to note that 'physiological feeling', or *physiological correlates of sentience*, in this context, are *not identical* to *homeostasis* but relate to *the reaction or response* of living systems to *changes* in homeostasis caused by sensory stimuli or other perturbations. The *reaction* of the system leads to the formation of consciously experienced *contents*. My hypothesis is that conscious cognitive and emotional experiences are the *expression* of a type of temporal process in which:

1) There is a deviation from homeostasis caused by an internal or external stimulus,

2) There is a reaction of the system to this deviation, on the basis of a capacity to recover homeostasis (‘allostasis’). *This reaction is the affective drive* that is typical of sentience;

3) The reaction *produces* consciously experienced *qualia* (sensations, affective and emotional states), which may be *anoetic* or *noetic*. Cognitive consciousness includes a *quale* called ‘the feeling of knowing’ (Burton, 2008);

4) The conscious experience motivated by the above reaction triggers a process of thinking with mental representations that we call *cognitive consciousness*, allowing the *projection* of representations supporting adaptive actions of the agent (the ‘self’) in the environment (the ‘world’).

While the complexity of the concept of feeling has gone almost unnoticed in consciousness studies, the very concept of consciousness has been discussed intensive and extensively, with a small contribution from this author on definitional and taxonomic approaches (Pereira Jr and Ricke, 2009; Pereira Jr. et al, 2010).

The construction of the ‘phenomenal’ domain of conscious experiences, departing from the ‘cognitive consciousness’ model, was developed with the ‘theater’ metaphor (Baars, 1997, partially reviewed in Baars, 2019). Another approach to phenomenal consciousness was constructed from the combination of Phenomenology and Neuroscience, in the *Neurophenomenological* approach. According to one of the branches of this approach, the Projective Theory (Velmans, 1990, 1993) re-elaborated by this author (Pereira Jr., 2018), the phenomenal domain involves temporal episodes in a egocentric space structure with qualitative states (*qualia*), and structured on two projected ‘poles’, called *Noetic* and *Noematic* by Husserl, and renamed *the Sense of Self* and *the Sense of World* (Pereira Jr., 2018). The use of ‘Noetic’ here is the same of Panksepp and colleagues.

In Pereira Jr. (2018), the Sense of Self is generated within the conscious experience; the Sense of Self is the *concept* of the entity (the “experiencer”) who feels and acts on the World. The Sense of World is composed of cognitive representations motivated by - and attended according to - the affective drive, and then ‘projected’ to the world of action. The projection of the two poles by the nervous system, interacting with the environment, forms complex spatiotemporal *episodes* filled with *qualia*. These qualia are composed not only of the cognitive representations themselves (in the previous example, the conceptualization of the properties of a sandwich) but also of the *expression* of the affective drive: the actual sensations, affective states and emotional feelings that guide the appraisal of the cognitive object (the ham is tasteful for the carnivorous, and disgusting for the vegan).

According to my approach (Pereira Jr.et al, 2017), the formation of full conscious episodes requires cognitive and enactive operations, such as the binding of features and decision-making. *Sentience* refers to the unstructured 'here-and-nowness' with many potential outcomes, while *cognitive consciousness* refers to structured conscious episodes with a Sense of Self and a Sense of World, and filled with representations having qualitative properties (*qualia*). The consciously experienced qualities (*qualia*; e.g. perceptual multimodal scenes) are properties of the World in the first-person perspective of the Self. For instance, my feeling of tooth pain is a property of the world as it is sensed by me; in this case, the 'world' includes parts of my body and everything else that I am conscious of, except my inner Self who experiences them.

On a side comment, I note that the above concept of cognitive consciousness is contextual or 'embedded', because the projection of the Self and the World require the 'here-and-nowness' being to be able to 'feel what happens' (Damásio´s expression) in the domain of interaction with the environment, co-generating cognitive contents by means of perceptual processes, and/or representing possible worlds on the basis of memories of previous experiences. This view overcomes the controversy of *Internalism* against *Externalism* in the Philosophy of Mind (reviewed in Wilson, 2017).

On the basis of the above clarifications and conceptual elaborations, in the next section I address the physiological correlates of sentience, preparing the terrain for the proposal formulated in the following sections.

Psychophysiology of Sentience

Recent progress in neurobiological research has pointed to the following operational structure of Sentience in the animal brain:

Stimulation-> Sensory processing in neurons-> Activation of the astrocyte network -> Control of the homeostasis of the extracellular 'Chemical Soup'-> Physiological Feelings (Sentience) -> Feedback on the neuronal network-> Behavior.

This dynamics of sentience is adaptive, not restricted to the Central Nervous System (CNS), but composed of whole-body interoceptive cycles that involve, in the human species, the enteric and cardiac nervous systems (Azzalini et al., 2019) with their inputs from and outputs to the CNS, and active striate muscles with kinesthetic sensors. *Somatic Marker Theory* (Damásio, 1994) and the *Adaptive Homeostasis Theory* (Shin et al., 2009) refer to whole-body processes activated in the interaction with the environment. These theories contrast with the traditional Cannon-Bard view of neural regulation of body-energy homeostasis, which is focused on internal feedback signals integrated in the hypothalamus and brainstem (Shin et al., 2009). In the broader approach of Shin et al. (2009) to energy homeostasis, besides the activation of behavioral, autonomic, and endocrine pathways, "these internal signals encoding energy status have much wider effects on the brain, particularly sensory and cortico-limbic systems that process information from the outside world by detecting and interpreting food cues, forming, storing, and recalling representations of experience with food, and assigning hedonic and motivational value" (Shin et al., 2009). Agreeing with this statement, I also claim that sentience is not limited to subcortical structures, or to neocortical structures; rather it involves cycles of homeostatic control in the whole neural tissue, by means of an action on the 'chemical soup' in which it is bathed (considering that in current usage by biologists 'neural' refers to the whole tissue formed by both neuronal and glial cells, also including the extracellular fluid and matrix).

Central to the control of homeostasis, in plants and animals, is the role of ionic waves. They are generated by changes in electrochemical brain activity, and feedback on the activity (see Busikla et al., 2019). Although plants do not have specialized neuronal or glial cells, they display similar adaptive homeostatic mechanisms: glutamate-induced calcium waves around the xylem and phloem (Toyota et al., 2018). These waves compose the "plant neural system" that controls adaptive processes.

The control of homeostasis in animals, generating 'physiological feelings', involves a large signaling network, which includes interoceptive somatic loops by means of blood flow signaling, as indicated in Figure 1.

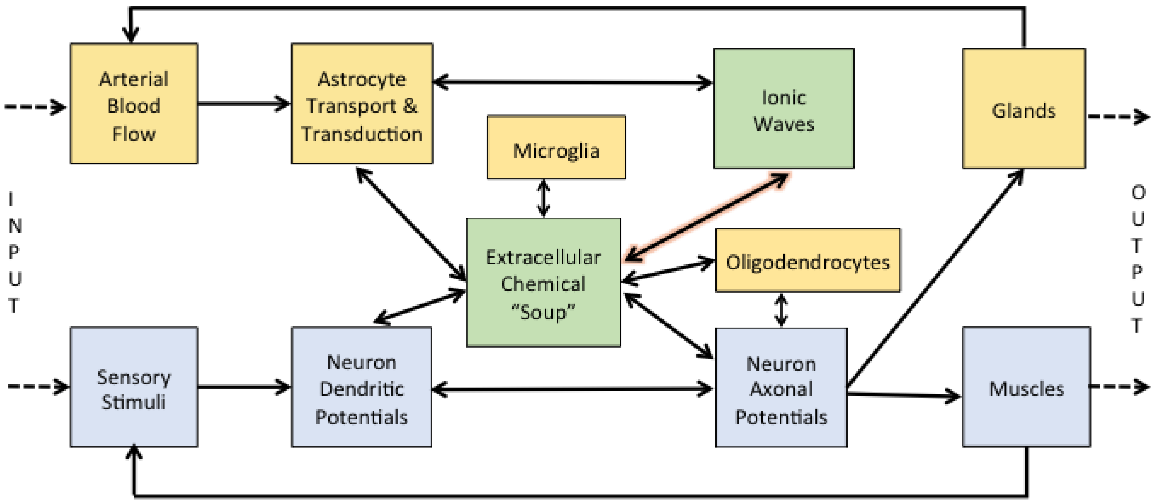

Figure 1: Physiology of Sentience in Neural Tissues. The 'Chemical Soup' includes Ions, Water, Transmitters, Neuromodulators, Hormones, Neuropeptides and the Extracellular Matrix. The homeostasis of the Extracellular Chemical Soup is controlled by the Ionic Waves. Allostasis occurs in the domain of the dynamical rapport of these two subsystems integrating signals from the whole circuits. Legend: a) Green: Structures and functions involved in basic processes of sentience, common to all multicellular living systems and colonies of unicellular living beings; b) Orange: Structures and processes involved in sentient processes proper to animals, based on blood flow interoceptive looping, and c) Blue: Structures and processes involved in cognitive processes based on neuromuscular loops and - in the human species - the capacity for inhibitory control of the epigenetic affective drive by neocortical circuits. Original figure made by APJ.

My concept of 'sentience', resulting from such structural and functional considerations, has strong psychophysiological foundations, formulated in four statements below:

1) Sentience is a type of dynamics in living tissues. The process has three phases: basal homeostasis (a stable state), the deviation from homeostasis caused by external or internal stimuli, and the recovery of homeostasis (called 'allostasis'; see Copstead and Banasik, 2013 and Pace-Shott et al., 2019). Sentience is not identical to basal homeostasis, neither to the recovery of homeostasis; rather sentience is the *capacity* of controlling the system to promote the recovery of homeostasis, or, in other words, sentience is *the capacity of allostasis*;

2) For evolutionary adaptive reasons, the exercise of the sentient capacity, besides its functional roles, *also generates conscious feelings*. Following Baldwin (1896), I

propose that sentience and the resulting conscious feelings of pleasure and pain guide adaptive behavior in response to changes in the body and environment. For instance, the experience of pain protects us from aggravating an injury, and the experience of pleasure guide us towards survival and reproductive behaviors. Cannon (1915) further related emotion to the action of chemicals that control homeostasis in neural tissue (e.g. noradrenaline). Giving an example, I mention thirst and satiation (Saker et al., 2014). Decrease of water concentrations in the body and proportional increase of salt in the blood leads to signaling to neural tissue that generates the thirst sensation, which guides the system to drinking behaviors and then the recovery of water-salt homeostasis. The ingestion of water up to satiation is accompanied by a pleasant conscious experience;

3) Ions are the vehicle for (biochemical) allostasis in neural tissue (and other tissues), as reviewed by Rasmussen et al. (2020): "interstitial cations (K+, Ca2+ and Mg2+) are not static quantities but change dynamically across states such as sleep and locomotion…these state-dependent changes are capable of sculpting neuronal activity; for example, changing the local interstitial ion composition in the cortex is sufficient for modulating the prevalence of slow-frequency neuronal oscillations, or potentiating the gain of visually evoked responses… the brain uses interstitial ion signaling as a global mechanism to coordinate its complex activity patterns, and ion homeostasis failure contributes to central nervous system diseases affecting cognitive functions and behavior" (Rasmussen et al., 2020);

4) Astrocyte transporters, astrocyte ionic (Ca+/Na+) intracellular waves and their extracellular effects (on K+ concentrations, Glu, GABA, and others) compose a mechanism that controls brain tissue homeostasis (Verkhratsky and Nedergaard, 2019). The release of calcium ions from the endoplasmic reticulum of astrocytes is central to the formation of these waves. The concept of *Hydro-Ionic Waves* (Pereira Jr., 2017) was proposed as an explanatory mechanism for the formation and propagation of bioelectric waves in neural tissues, corresponding to a psychophysiological substrate of sentience.

Although it is well known that the triggering of some sensations and feelings is made by specialized structures – e.g. fear is related to the activation of the amygdala (LeDoux, 2000), and pain to the activation of parts of the insula (Isnard et al., 2011) – the four above statements imply a systemic effect, involving neuro-astroglial signaling networks and ionic waves crossing living tissues. In the next sections, the above scientific concepts of sentience and physiological substrates are applied to practical issues in Neurology and Psychiatry.

Sentience in Neurology

The distinction between sentience and cognitive consciousness, beyond conceptual issues and semantical and terminological implications, has important scientific and practical implications for Neurology. In the previous section I have briefly reviewed recent results in Physiology that support the claim that sentience relates to the *control* of chemical homeostasis, promoting *allostasis* (the recovery of homeostasis after perturbations). In this section, I suggest several applications of this knowledge in Neurology.

When we are awake and sentient, physiological mechanisms such as glial transporters and calcium waves control chemical homeostasis, making available substances like lactate, glutamate, noradrenaline, acetylcholine, dopamine, serotonin, neuropeptides and many others, in concentrations that allow dynamic responses to stimulation. The state of this complex biochemical system is critical for the possibility of formation of bioelectrical patterns necessary for conscious experience, as the synchronization of neuronal activity following a proportional distribution of EEG wave frequencies. For instance, the dominance of delta waves is typical of unconscious states in deep sleep, while a combination of faster rhythms and amplitude modulation in time – as revealed by event-related potentials - is typical of conscious states (Pereira Jr. et al., 2017).

As the proper correlates of consciousness extend beyond the most basic correlates of sentience, the former cannot be taken as a general parameter for the detection and intervention on the latter. A major concern of medical procedures during general anesthesia, palliative care and clinical interventions to improve the quality of life is if the person being treated *can* feel pain in the presence of a noxious stimulus. The *capacity* of the person to feel pain, even if there is no noxious stimulus (and she is not consciously experiencing pain) belongs to sentience, while the cognitive and emotional experiences of actually feeling pain belong to the 'phenomenal' domain of consciousness. In the same vein, the capacity to feel hunger - if there is a lack of food - or to feel thirst - if there is a lack of water - indicates that the person is sentient, while actually experiencing the *qualia* of some food or drink belongs to conscious experience.

Additionally, if the object of experience is cognitively represented, it is a case of *noetic* or cognitive consciousness. If it is *not* cognitively represented, as in the case of vague feelings or emotions, then we have an instance of *anoetic* consciousness, but once we give a name to the feeling or emotion, it becomes - *a posteriori* – attached to a representation. This philosophical issue is relevant for Neurology in situations when a person is asked to describe what she felt during a surgery under general anesthesia. She may give a cognitive report, naming her sensations, on the basis of the memory that was formed and retrieved, although she had no cognitive representation of the feelings *at the occasion she experienced them.*

The representation of the object of experience (e.g. bread with cheese and ham) belongs to the narrow branch of experience called ‘cognitive consciousness’. This high-order phenomenon cannot be taken as the general standard for neurological diagnostic and treatment, because it covers only part of the physiological processes of conscious experience. Taking sentience as the most basic capacity necessary for conscious experience allows a broader medical approach to the physiological processes that make consciousness possible.

General anaesthesia is often characterized as a *loss of (cognitive) consciousness,* for example, as the incapacity of forming memories of pain during a surgery. However, if the main criterion is not being capable of *feeling pain*, then its effects extend beyond the absence of cognitive conscious experience of the medical event (e.g., invasive surgery) and episodic memory about what happened during the event. In other words, the goal of general anesthesia – abolishing for some time, during a surgery, the capacity of feeling pain - would be broader and more important than the absence of cognitive consciousness; ‘not being able to feel pain’ in the *presence* of a strong noxious stimulation implies not only the absence of cognitive representations of the pain, but *the absence of any conscious pain sensation or emotion*.

An important finding in regard to the physiological correlates of general anaesthesia and the corresponding loss of sentience is the role of glial cells in continuous transmission of hydro-ionic waves in neural tissue. Most researchers agree that cognitive consciousness in human neurobiology involves neocortical circuits of spiking neurons; however, the action of three common anaesthetics is mostly on glial cells, specifically the astrocytes (Thrane et al., 2012). An additional finding implying that sentience is a tissue phenomenon relatively independent of the neuronal spiking is the discovery that tissue electromagnetic waves related to sentience can propagate without neuronal axonal transmission, pointing to the involvement of the astrocyte network (Chiang et al., 2019; Martinez-Banaclocha, 2020).

Astroglial dysfunction, such as the defective propagation of ionic waves, implies the incapacity to control the deviations from basal homeostasis towards recovering stability – or, in other words, the incapacity for allostasis – corresponding, in the theoretical framework introduced here, to a loss of sentience. The *astrocytic syncytium* is the network composed by large populations of astrocytes inter-connected by gap junctions, forming a continuum 'master hub' in which ionic waves propagate (Pereira Jr. and Furlan, 2010). The *isopotentiality* of the astrocytic syncytium, allowing the flow of ions in all directions upon local stimulation, is crucial for *allostasis* (Ma et al., 2016; Kiyoshi et al., 2018). If the flow is not isopotential, the consequence is that some parts of the brain are not integrated in the allostatic process, while other parts are overloaded. Considering the central role of astrocytes in brain allostasis, Verkhratsky et al. (2016) concluded for "the pathogenic potential of astrocytes in a variety of disorders, ranging from neurotrauma, infection, toxic damage, stroke, epilepsy, neurodevelopmental, neurodegenerative and psychiatric disorders, Alexander disease to neoplastic changes seen in gliomas".

One important neurobiological feature of energy usage in the brain is the fact that the glucose carried in arterial blood flow is mostly delivered to astrocytes, not directly to neurons. Astroglial cells process glucose from the blood into the 'lactate shuttle' (Pellerin et al., 1998; 2007) and deliver the product (the lactate) to neurons, where it is further processed into ATP and cyclical AMP, for consumption in cellular metabolism and in the dynamic control of homeostasis. This astroglial function is central to the differential circadian cycle delivery of energy to neurons, corresponding to the functional distinction of non-dreaming sleep and wakefulness. Research on neuron-astrocyte interactions in the last two decades has produced experimental evidence that the lactate that circulates in the extracellular milieu and reaches neurons (Petit and Magistretti, 2006) supports the waking state and related sentience. Considerations about how useful energy is processed in the brain and used to reduce thermodynamic entropy are central to the understanding of the psychophysiological states of sleeping and dreaming (Hobson and Friston, 2012). The role of astrocytes in energy metabolism is part of a larger process of energy consumption related to neurological recovery (Stender et al., 2016). According to Bojarskaitė et al. (2020), calcium signaling in astrocytes is “sleep-wake state specific”, which suggests that the lactate shuttle and the resulting amplitude-increased calcium waves (up to a threshold, beyond which an epileptic seizure may happen) can be taken together as *a biomarker for sentience.* Ingiosi et al. (2020) registered changes in astroglial calcium waves in REM, Non-REM sleep and wakefulness, showing (in three videos) a sharp increase in the amplitude and synchronization of the waves in the sleep-wakefulness transition.

In the transition from sleep to wakefulness, there is a sharp rise on the amplitude (vibrational kinetic energy) of calcium waves, as shown in videos 1 and 2 of the cited paper (Ingiosi et al., 2020), making the system able to feel (*sentient*). This phase indicates that the system can “feel what happens” but is not itself the correlate of a specific experienced feeling. The correlates of specific feeling experiences appear in the next phases of the calcium signaling during wakefulness, as in the case of conscious tasting experiences registered with calcium imaging using two-photon microscopy and implanted microprisms (Chen et al., 2020.)

The above findings have important implications for neurological diagnostics and therapy. The connection between lactate, astroglial calcium waves and the control of neural homeostasis (Verkhratsky and Needergaard, 2019) is still not well known in the medical community but opens new possibilities of intervention. For instance, lactate concentrations in cerebrospinal fluid (CSF) samples can be used in medical practice as a biomarker for sentience. Needergaard and colleagues found evidence for what they called the ‘glympathic’ system, composed of channels for the circulation of cerebrospinal fluid in neural tissues, contacting glial cells in the brain. The above-mentioned ‘lactate shuttle’ is carried by this system. While we are awake and sentient there is an increase of lactate levels in glympathic pathways, while the lactate concentration decreases when we are in deep sleep (Lundgaard et al., 2017). This system is critical for neurological evaluation of the capacity of generating conscious states and experiences, because a defective flow of lactate in the glympathic system would impair sentience, while adequate levels of lactate during wakefulness imply that sentience is intact.

Lactate concentrations as biomarkers for sentience provide a new technique to measure the minimal level of activity necessary for conscious experience, for people in the 'vegetative' state. In a recent study the authors say that “We are establishing a biobank (blood, cerebrospinal fluid and brain tissue, where available) to facilitate future genomic and microbiomic research to search for signatures of consciousness recovery" (Skibsted et al., 2018). While there is a positive correlation between increase in lactate concentration levels and sentience, changes in concentration of other CSF macromolecules (such as melatonin and adrenaline) do not seem to be directly and specifically related to sentience but – of course – further investigations are needed to find the best combination of signals to serve as a biomarker. As a working hypothesis, adequate lactate concentrations in 'vegetative' state patients would indicate greater probability of recovering full consciousness.

'Absence epilepsy' refers to the *loss of sentience* causing a loss of consciousness, determined by events in the domain of neuron-astrocyte interactions (Diaz Verdugo et al., 2019). These events involve a defective function of GABA transporters in astrocytes (Crunelli et al., 2013), accompanied by an increase in calcium waves (Fellin et al., 2006) and slow outward currents of calcium from astrocytes to neurons (Kozlov et al., 2006). These factors generate an increase in the amplitude of dendritic potentials and in axonal firing rates that result in the well-known 'spike and wave' bioelectrical phenomenon in epilepsy (an increase in the amplitude in scalp EEG registers, displaying bioelectrical peaks), clinically and experimentally measured for more than half a century. These findings have inspired the suggestion of new treatments for epilepsy (Crunelli et al., 2015) - as well as for degenerative diseases such as Alzheimer's and Parkinson's (Finsterwald et al., 2015) - *targeting the astrocyte network*. The rationale for these proposals is that astroglia provide far more than a supportive system for neurons, having psychophysiological functions such as supporting wakefulness, providing the control of homeostasis (or *allostasis*), generating affective states experienced by the agent, and generating motivation for action.

One of the major challengers in neurological therapy is the suppression of CNS processing of somatic chronic pain. Acupuncture is widely used for this purpose but its therapeutic pathways remain controversial (Vickers et al., 2018); possibly, the type of energy involved in the procedures interferes with hydro-ionic waves in the CNS. With more explicit scientific foundations, but still poorly understood, the treatment of somatic pain with Transcranial Direct Current Stimulation (tDCE) also implies dynamic events in neural tissue. Considering that the 'chemical soup' is a bioelectrical conductive medium, the transmission of a current from two distant scalp sites implies the induction of interferences between the exogenous electric current and the endogenous hydro-ionic waves. In tDCE, the part of the electric current that is not conducted by the skin or the skull is assumed to pass through the CNS tissue, moving from one scalp location to another, thus interfering with the dynamic patterns of ionic waves and having other effects (e.g. on protein conformation) to generate the desired therapeutic results. The type of interference caused by the current is not well-known but there are good morphological and physiological reasons to believe that the transmission is not mediated by neurons, since these cells do not form a continuum; they are rather separated by synaptic clefts, in which the transmission of signals is chemical. The transmission of bioelectrical currents exclusively by the ‘chemical soup’ would be not sufficient to explain long-range directional phenomena. Therefore, as the tDCE current find ways to move between (relatively) long distances through neural tissue, the most probable pathway is through the chemical soup reaching the astroglial network (Monai et al., 2016; Monai and Hirase, 2018), because these cells, contrary to neurons, are connected by gap junctions forming a continuum (Kiyoshi et al, 2020).

There are many findings about the application of tDCE for the treatment of neuropathic pain (for a review, see David et al., 2018) and somatic abdominal pain (e.g., Bayer et al., 2019). These treatments do not target the neocortical specialized circuits thought of as being the neural correlates of cognitive representations; they instead interfere with dynamic bioelectric waveforms present in neural tissue.

In neurological rehabilitation, targeting the whole neural tissue is also implied by the use of rotating magnets in the treatment of ischaemia and stroke. The effect of rotating magnets on brain activity was discovered by Ross Adey in the 1950’s (his work was reviewed by Oransky, 2004). Adey tried several types of noninvasive magnetic stimulation, but only moving magnets caused a consciously detectable effect. This finding was forgotten for a long time but deserves to be recalled after a research group from the Methodist Hospital in Houston (Texas, USA) found that powerful rotating magnets are effective in the treatment of stroke and ischaemia (Helekar et al., 2018). The inference that can be made is that the rotating magnets, although possibly not directly affecting conscious cognitive representations, do impact the structures and functions of neural tissue that support sentience, thus making possible the recovery of full conscious functions. This is not a conclusive result, but a promising new area of investigation that deserves further investigation, possibly leading to new, portable technological tools for neurological therapy that can be used at home - an advance in comparison with the big and heavy coils for transcranial magnetic stimulation, which are available only at the specialized hospital.

Sentience, in this perspective, becomes co-extensive to *arousal* (Duffy, 1972), the basal activity referred to by Seth (2019) as the lower level of consciousness, but *not necessarily* implying a 'general arousal pattern' of activity, or a CNS state devoid of specific physiological correlates for each emotion. The latter view is proposed by theorists who understand that the specification of an emotional state is made by external social factors. Instead of a 'general arousal pattern', I argue for the existence of different types of 'central states', corresponding to each type of consciously experienced emotional phenomenon; in other words, for every type of emotion there should be a specific dynamic electrochemical pattern being instantiated in the CNS. This relation between mental and physiological states is, of course, a philosophical issue, but the conception that is assumed influences how emotional processes are interpreted and treated in medical practice.

Barrett (2017) has argued, against the 'central states' view, that the specificity of emotions results from the social contexts where and when they are elicited. I agree with her about the relevance of social interactions for the generation of specific emotions, while holding that the *affective drive* of each species and individual includes 'templates' (ontogenetic patterns) for the expression of emotions. The interaction with the environment selects which template becomes actual at each moment. For instance, the fear of scorpion is somehow hard-wired in human individuals, even those born in urban concentrations - who have never interacted with scorpions in their whole lives. The *medical* concept of arousal, in the perspective assumed in the theoretical framework proposed here, includes a range of specific possibilities for emotional expression, which may become actual depending on the specifics of the interaction of the agent with the social context.

Only when we are sentient, awake-and-feeling, can we be conscious of ourselves and of the world, but *sentience itself is not a consciously experienced feature*; it is a *here-and-nowness* with a range of possibilities to be actualized and filled, in normal conditions, with cognitive and emotional conscious features related to the interaction with the physical and social environment. In abnormal conditions caused by neurological conditions, *there may be sentient arousal without the formation of fully structured conscious episodes*. Should the human person in this condition be considered less valuable or deserving of treatment, than in the state of elaborating on conscious cognitive representations?

Sentience in Psychiatry

During general anaesthesia, as during coma, absence epilepsy, or, more frequently, during dreamless slow-wave sleep, there is a loss of sentience. When we are awake, we are sentient – but may not be fully conscious or may suffer from mental disorders that affect how we construct conscious episodes. While neurological lesions and dysfunctions have their basis in the impairment or loss of sentience, disorders of conscious functioning involve other physiological correlates and corresponding mental phenomena. However, as consciousness is dependent on sentience, changes in the personal ways of feeling - the individual's 'affective drive' – should have an impact on psychiatric disorders. For instance, in anxiety disorders there is a phenomenon that may metaphorically be conceived of as a 'shrinking' of the *here-and-nowness,* possibly corresponding to a decreased capacity to control homeostasis. In bipolar disorders, the mechanism of action of lithium (which is, physically, a substitute for endogenous cations) putatively impacts the physiological correlates of sentience, facilitating the induction of *allostasis* by the astroglial calcium wave (Rivera and Butt, 2019), thus reducing the intensity of euphoric and depressive phases.

According to this perspective, disorders of mood and anxiety are primarily disorders of sentience. The manifestation of 'symptoms' is shaped by the personal history and cultural patterns, both of which influence how the ways of feeling are consolidated in each person and then operate unconsciously. As the mechanisms of sentience are not under direct conscious cognitive control, the treatment of disorders requires the resources of physical (e.g. magnetic stimulation) and biological (e.g. pharmacological) therapies, as well as the resources of psychodynamics and behavioral training.

Even though sentience (which is key to psychiatric symptoms) is not under conscious control, it is impacted by past conscious experiences related to, for instance, religious faith and socioeconomic hardship. It is primed by psychosomatic, religious, spiritual, economic and political experience in complex ways that can be approached in several branches of Psychology, as the Jungian concept of a 'collective unconscious' (Hunt, 2012). The influence of such priming on the interplay of conscious emotions and cognition is central to all types of psychiatric disorders. In Freudian psychotherapy, the ways of sentience are classically understood as unconscious processes of the Id and Ego that influence emotional states and behavior (Freud, 1923). The influence is more salient in mood and anxiety disorders, but also identifiable in personality disorders and schizophrenia (for the role of glial cells in the latter, see Dietz et al., 2020).

In the perspective I have adopted here, cognitive representations cannot be fully understood without considering affective aspects of the history of the individual and the interplay with emotional processes (as discussed in my supplementary paper in this JCS issue about the *dizziness* I experienced during a virtual reality roller-coaster ride). These affective influences on cognition are claimed to underpin individual differences in visual and auditory processing. Depending on the previous experience and the motivation of different people, the vertigo they experience during a roller-coaster ride may be strong or practically non-existent.

This proposed approach to psychiatric disorders contradicts current assumptions in Cognitive Neuroscience, for which the brain correlates of cognitive consciousness (patterns of neuron connectivity and firing that instantiate mental representations) are conceived, for practical purposes, as independent from the processes of sentience. Cognitive representations are studied as the differential activation of neuronal circuits, or changes in neuron synaptic connectivity above a given excitatory threshold, as detected by functional magnetic resonance imaging and electroencephalography registers. This type of data is often assumed to be *sufficient* to explain the neural correlates of conscious cognition. The necessity of having a sentient being experiencing the representation for the representation to be conscious is often neglected.

Contrasting with this assumption, in the classical concept of 'knowledge' criticized by Plato, the existence of *beliefs* about the representation (and its linguistic expression) is considered a necessary component. The belief in a proposition is a sentient motivation for human linguistic behavior. Burton (2008) has argued, on an experimental basis, that the "feeling of knowing" is the main psychological component of a person's belief of knowing, even when what is believed is false.

The argument for the necessity of sentience for cognitive representations to become conscious can be formulated as follows. Any knowledge acquisition is a *triadic* phenomenon, composed of:

1) A mental representation, in the form of a statement, image or symbol;
2) The subject who experiences the representation as a cognitive intentional object; and
3) The referent, or the 'real' object the representation is about.

Assuming the below premises:

1) Sentience is constitutive of the being who elaborates and experiences mental representations;

2) The motivation that drives attention to focus on the referent depends on the person’s affective drive guiding the process; and

3) There is no knowledge without the knowing person focusing her attention on the referent,

then sentience *is necessary* for consciousness.

On the other hand, consciousness is *not necessary* for sentience; the proof of this statement is in the fact that the event of changing our representations about an issue has limited or no effect on changing the ontogenetic, personal ways of sentience. For instance, becoming conscious of chemical imbalances underlying a mental disorder is not sufficient to change the physiological correlates of sentience and promote rehabilitation. The relevance of sentience in psychiatric treatment implies the need to take into consideration the problems regarding the proper functioning of physiological correlates that impair or distort the formation of conscious cognitive and emotional experiences or interfere with the desired interaction of cognitive and emotional processes.

Assuming the validity of the above argument, the understanding of the physiology of sentience becomes relevant to Psychiatry. As the control of homeostasis in neural tissue is mediated by astrocytes (Verkhratsky and Needergaard, 2019), effective physical and biological therapies for psychiatric disorders should target the physiology of astrocytes. According to Kim et al. (2018), “general findings indicate decreased astrocyte cellular features and gene expression in depression, chronic stress and anxiety”.

Therapies targeting astrocytes (Peng et al., 2014) are likely to complement existing therapies based on pharmacological drugs that bind to neuronal receptors, but it should also be taken into consideration that astrocytes have the same receptors and may be activated by current drugs designed to target neurons. A typical case is ketamine, which has long been known to exert a dose-dependent strong effect on consciousness (Pereira Jr. and Johnson, 2003), generating hallucinations (in low doses) and general anesthesia (in higher ones). These effects are likely to be mediated by binding with both astroglial and neuronal receptors, but until recently only the latter have been focused in scientific research.

Stenovec et al. (2020) discovered a neuro-astroglial mechanism of the antidepressant action of ketamine through the activation of the inositol triphosphate pathway inducing astroglial calcium waves, which prompt the action of potassium ions on neuronal membranes. It is well known that neurotransmitter transporters (proteins that carry macromolecules through membranes and/or to specific cellular compartments) are important in Biological Psychiatry (Iversen, 2006). New types of drug can be designed to target *astroglial* transporters (for their structural position, see the diagram of Fig. 1), opening the doors to a new field of research and pharmacological intervention: the medical treatment of mental disorders acting on astrocytes and neuro-astroglial interactions (for a review, see Pereira Jr., 2017), as well as on other glial cells (tanycytes, microglia and oligodendrocytes – see Garcia-Caceres et al., 2019).

I hope the line of reasoning pursued in this section leads the reader to delve further into the emerging field of glial Biological Psychiatry; for an overview of glial cells in medicine, the reader is referred to Douglas Fields (2009).

Concluding Remarks

The main contributions intended in this target paper are:

1) The conceptual distinction of sentience and cognitive consciousness;

2) Identifying their different neural correlates, and

3) Arguing for medical approaches that take sentience into consideration.

As a result of these developments, I hope to make the case that sentience could be an important operational concept in Neurology and Psychiatry.

Although sentience is the basis for consciousness, philosophically speaking the concepts refer to two different *modes of being*. Sentience is a *dispositional* category, while Consciousness is *actual*. Conscious contents (sensations, emotions and cognitive representations with qualia) are *expressions* of the potentialities of sentience. For instance, hunger (the *capacity* of feeling hungry) belongs to sentience, while the *experience* of feeling hungry (because there is a stimulus operating – an empty gut signaling to the brain) belongs to consciousness. When we think with mental representations about the objects and processes of experience (as in the case of the desire of eating a sandwich of cheese and ham), then there is cognitive consciousness. If there is also an emotion attached to the representation (e.g. pleasure), then there is full consciousness with both cognitive and emotional experiences.

Another difference that is relevant to Epistemology concerns the method of investigation of the related phenomena. On the one hand, sentience, as the capacity of controlling homeostasis with the generation of adaptive feelings, can be studied by means of *biological structures and functions*, as empirical registers of ionic waves and the lactate biomarker. On the other hand, conscious first-person experiences in episodes containing mental representations and with attached *qualia* cannot be reduced to their biological correlates, neuron firings and patterns of connectivity, as famously claimed by Chalmers (1995). They can be accessed by means of qualitative reports by the subjects, but this source of information is lost or reduced in neurological and psychiatric conditions.

Distinguishing the physiological correlates of sentience and cognitive consciousness has important medical implications for the ways of diagnostics and treatment in medicine for patients in 'vegetative' states. The claim that the capacity of elaborating mental representations is less fundamental to the evaluation of conscious activity than the capacity for sentience, if true, could have a significant impact in medical practice and bioethical considerations. The minimal requirement for considering a person conscious is, according to this line of reasoning, if she is *capable of feeling* basic sensations such as hunger, thirst and pain. Higher-level capacities, such as imagining playing tennis (a technique for assessing residual consciousness in vegetative states – Owen et al., 2006), may not be adequate as a *general standard* for medical diagnosis of disorders of consciousness, since – according to the proposed reasoning – in many cases the person may not be able to perform well in these tasks, but still be capable of consciously experiencing basic sensations such as hunger, thirst and pain, in the presence of the corresponding endogenous or exogenous stimulation. As a result, instead of 10% of persons in a vegetative state being conscious (Monti et al., 2010), there may be far more of them being sentient. This possibility has important bioethical implications.

Focusing on sentience implies that there may be biomarkers useful for diagnosis, and new ways of treating disorders of sentience (such as chronic pain) and emotional consciousness (such as depression and anxiety) by means of electric and magnetic stimulation addressing the glial network. Another possibility is the development of new chemicals to be delivered through the glympathic system, addressing glia instead of neurons. In sum, the development of this field of investigation in Neurology and Psychiatry can bring new methods for diagnosis and therapies addressing the neural correlates of sentience and its conscious – cognitive and emotional - expressions.

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