OPINION ARTICLE

The necessity of studying higher brain functions from a first-person frame of reference [version 1; peer review: 1 approved, 1 not approved]

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Abstract

Almost all higher brain functions are first-person properties and anyone seeking to study them faces significant difficulties. Since a third-person experimenter cannot access first-person properties, current investigations are limited to examining the latter by using third-person observations that are carried out at various levels. This limits the current studies to correlational experiments using third-person observed findings. In order to initiate a study of explanations for the first-person properties, experimental approaches should be undertaken from the first-person frame of reference. But, there is a huge barrier. I discuss my opinion for crossing this barrier using a three-stage approach – theoretical, computational and experimental – in that order. These stages will naturally lead to the gold standard of understanding the mechanism by replicating it in engineered systems. The hurdles and incentives of undertaking this approach are discussed.

Keywords

first-person sensations, first-person frame of reference, higher brain functions, semblance hypothesis, third-person observations, artificial intelligence

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Introduction

Attempts to interconnect third-person findings obtained at different levels such as biochemical, cellular, electrophysiological, systems, imaging and behavioral studies by different fields of neuroscience remains a challenge^{1,2}. In contrast to other systems in the body, nervous system functions are unique in that all the higher brain functions are first-person properties of the mind. These functions include the state of being conscious, the ability to perceive sensations, the ability to internally sense retrieved memories and the ability to generate thoughts (Figure 1). Only the owner of the nervous system has access to these functions, making them purely first-person internal sensations³. First-person reports of these sensations through motor activity such as behaviour and speech provide surrogate markers to the third-person observers. Currently, clinical evaluation of neurological and psychiatric diseases is based on assessing the first-person reporting and third-person observed findings. This severely limits our understanding of a) internal sensations in non-responsive patients, b) defects in the mechanism of formation of the internal sensation of memory, and c) the compelling sense of reality of hallucinations in psychiatric disorders. The surrogate markers for assessing the first-person properties may not represent the true nature of the internal sensations. This is because a) behaviors may be altered due to changes in the circuitry, or b) some species of animals may voluntarily hide the truth and exhibit behaviors misrepresenting them. Similarly, almost all the current approaches use third-person observed findings at various levels⁴ in correlational studies with surrogate makers of biochemical changes, neuronal activations, oscillating potentials, signal changes in imaging studies, and behavioural responses to connect with the first-person properties. Another important area of study is to understand consciousness⁵. An entire branch of medicine that deals with blocking this first-person property of consciousness – anesthesiology – requires knowledge of its mechanism due to several reports of neurodegenerative diseases associated with anesthetics⁶.

Current third-person studies at various levels assume that first-person internal sensations are emergent properties of the system. Emergence can be adopted as a framework to study properties that cannot be explained using the third person-observed features of the system. However, reductionism can be used to carefully examine the factors upon which the emergent properties are dependent and hypothesize the smallest possible structure-function unit from which internal sensations can be induced. Therefore, views of emergent properties and reductionism can be seen as mutually inclusive. By using them in conjunction, first-person internal sensations can be approached.

Converting first-person sensations to third-person features

The first-person features of the higher brain functions cannot be studied in biological systems due to access issues. Recent research work is attempting to overcome this barrier by approaching higher brain functions from a first-person frame of reference, examining the locations and mechanisms that can lead to the formation of the basic units of internal sensations^{7,8}. This drastically different approach is based on the view that the gold-standard test of understanding the formation of first-person internal sensations is to replicate the mechanism in engineered systems. This approach is being carried out in three stages. The first step is the theoretical derivation of the basic functional units of the system at the correct level that is also connected to the motor system, which can explain all the higher brain functions along with behavioral motor activity. It is found that a) locations from which memories can be retrieved gradually shift from the hippocampus to the cortices over several years, and b) patients recover completely after suffering from small strokes at certain locations of the brain. These suggest that the basic structure-function units are spatially definable and transferable, and that emergent functions can be integrated from multiple locations. Since a large number of functions and loss-of-function states for the system are being studied by different faculties of brain sciences, the

Figure 1. Frame difference between the first- and third-person views of the nervous system functions from different levels. Third-person observed features include neuronal firing, electrophysiological changes and surrogate markers of internal sensations such as behavioral motor activities and language. It has not been possible to interconnect between different third-person findings. Hypothesizing the mechanism of first-person internal sensations of different higher brain functions capable of interconnecting various third-person observed findings is an optimistic step towards verifying the first-person view.

solution capable of explaining both the first- and third-person properties is likely a unique one. In other words, there is only one solution. Therefore, theoretical work to hypothesize structure-function units is the first major step. The second step is to carry out computational studies to examine the nature of the algorithms for different modules of functions that can result in expected qualities for the generated internal sensations. The third step is to build engineered systems that can provide readouts of the formed internal sensations based on the rules by which they are built (Figure 2). It is likely to require combining the second and third steps.

Focal points of emergence

Of all the third-person sensed findings, neuronal firing (also known as somatic spikes) can be easily observed, induced and measured. New tools to make the firing of neurons visible provide an advantage in examining the nervous system from the third-person frame of reference. Somatic spikes are one of the different kinds of spikes observed along the neuronal processes. Others are dendritic spikes and axonal spikes. Most importantly, the potentials originated by the dendritic spike at farther locations degrade as they arrive at the neuronal soma. When examined from the third-person frame of reference, it can be seen that a very large number of excitatory postsynaptic potentials (EPSPs) are not being used efficiently to justify their evolutionary preservation. For example, EPSPs during sub- and supra-threshold activations of a neuron are not contributing to any function. Contribution of potentials from synaptic events that occurs remote from the neuronal soma towards neuronal firing is minimal⁹. Is there a different view possible for their functional

attributes? The evolutionarily well-preserved occurrence of all the synaptic potentials, in surplus to what is required for the observed neuronal firing, prompts some important questions. What functional significance can they impart when examined from a first-person frame of reference? For such investigations, the most important question is “At what focal points in the nervous system do the units of internal sensations emerge?” These approaches are expected to ultimately guide the discovery of units for the generation of internal sensations.

The gold standard

The gold standard for understanding the operational units requires transferring the theoretically-derived operational mechanism in engineered systems. Since internal sensations are virtual in nature, the conversion of the formed internal sensations into third-person observable outputs is indispensable to understanding the operation. In this context, the main limiting step is the theoretical derivation of the basic operational unit, at the correct level, that can explain all the nervous system functions from both first- and third-person frames of reference. This is followed by replication of the mechanism in engineered systems similar to that which are proposed¹⁰. Studies of first-person systems will deal with optimizing the properties of the components of the engineered system by seeking specific experimental results from biological systems. These studies will require regular feedback from computational studies to solve optimization problems. Finally, the studies are expected to arrive at the algorithms that can provide the desired outputs. At the advanced stages, the systems science will examine the systems properties from a

Figure 2. Steps required to cross the barrier of frame difference between the first- and third-person functions. Diagram shows a path for the first-person scientific approaches for replicating theoretically feasible hypothesized mechanisms in engineered systems. The readouts obtained from these systems can be used by third-person experimenters to fine-tune the internal sensations to match with both the expected internal sensations and behavioral motor activity. An inevitable end-product of this approach is the development of artificially intelligent systems.

holistic view, including its interaction with surrounding environment and dynamic behavior through complex paths that are reinforced during certain operations. In addition, the systems science will be able to examine instabilities when the system crosses the “boundary conditions” that can mimic the disease process. Systems design, systems development, systems stability, systems analysis, systems dynamics, and systems viability will become necessary elements of this process.

Major hurdles

There are two major obstacles in exploring the first-person properties of the nervous system. In my opinion they cannot be separated from the very challenge of discovering the first-person properties. The first one is reaching a consensus among researchers of one faculty of science for funding projects that involve significant changes in the research approach. If a logically-fitting experimental approach is available, then practical difficulties in conducting it should not deter us from undertaking it. Since the mechanism of the nervous system functions has not discovered yet, it is understandable that a novel approach is required. Changing the frame of reference from which to examine the higher brain functions suits such an anticipation. In my opinion, first-person approach should be brought into the main stream investigational methods in neuroscience. In fact, first-person studies should distinguish neuroscience from the studies of other organs in the body.

The second challenge is to maintain a certain level of confidence that we can discover the mechanism of formation of first-person properties. The necessity of discovering the mechanisms for the disorders of the mind should take precedence over the fear of discovering the operations of the mind. There is a growing concern about ‘the Singularity’, a threshold point above which engineered systems will become more intelligent than humans. The fear comes from the thinking that artificially intelligent machines may take over the human race. Building regulatory bodies and having strategies in place to prevent the development of these foreseeable effects should be simultaneously carried out along with the development of methods for exploring the first-person properties.

In conclusion

A reasonable early expectation from first-person studies is the development of experiments that can provide third-person-sensible outputs at key stages, so that data collection and exploration of

further work can become possible. Comparative physiology of the mechanisms of formation of first-person properties using different model nervous system circuitries will be part of this approach. The first-person studies will also aim to identify the focal points at which the mechanism is disrupted in neurological and psychiatric disorders. By taking advantage of the information arriving from first-person studies, we will be able to design methods to prevent and treat several neurological and psychiatric diseases.

The nervous systems of even very low-level species produce intentionality to carry out survival and reproductive instincts, indicating that an evolutionarily highly conserved mechanism is shared among all species of animals. The presence of nearly ten million existing and predicted animal species on earth¹¹ provides a great deal of confidence to successfully simulate the mechanism in engineered systems that mimic one of them. Such intelligent systems are of paramount importance to help aging populations with the care they need, design strategies to feed the hungry, cure diseases, alleviate human suffering and provide methods to prevent climate change, to name a few. My opinion is that the steps towards finding solution to the virtual nature of the first-person properties will have similarities to the development of complex numbers in mathematics. Therefore, first-person studies will fall into the realm of a completely independent new branch of basic science. The conclusion of this opinion article is that a first-person approach to understand the brain and the natural course of events that will lead to the development of artificial intelligence are two sides of the same coin. A discussion on this topic among neuroscientists, computational scientists, and engineers can spark many bright ideas.

Competing interests

Author has applied for a U.S. patent (application no: 14/068,835) of an electronic circuit model of the inter-postsynaptic functional LINK.

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Illposed answers to illposed questions

The manuscript raises a seemingly intriguing and provocative question about perspective taking in experimental Neuroscience. It argues that many daunting problems would benefit from a first-person frame of reference, both as a method as well as a subject at the same time. More specifically, the question has two main aspects: (A) One concerns with the method of studying neuronal functions from first-person versus a neutral (third-person) point of view, and (B) the other aspect concerns with the first-person ontology of consciousness. Unfortunately the confusion of these two aspects creates an ill-posed contradiction between third-person methods and first-person subject leading the author to questioning the adequacy of standard scientific method. Since the manuscript fails to disentangle the two aspects above, it necessarily fails to provide a tangible solution.

Main concerns:

A) Starting with the first-person methods:

1. Regarding the adequacy of third-person scientific method (aspect A): The third-person point of view is typically not a matter of choice. (Actually, the term "third-person" is imprecise, as it should be a depersonalized point of view.) The concept of "impartiality" is central in the philosophy of science. It has a huge literature and long history from Plato to Karl Popper. There are a number of good reasons why scientific investigations consistently attempted to dissolve the role of observer in scientific paradigms until physicists, including Einstein, Heisenberg, Schrodinger, Planck to name a few, showed that observations necessarily interfere with the observed system. Einstein in general relativity, inspired by Ernst Mach's conjecture (Von Baeyer 2001), approaches the limitation of "objectivity" as the dependency of measurements on the position and speed of the observer relative to the speed of light

and the time of observation. Acknowledging that there IS NO observation without interference, objectivity is asymptotic. Nevertheless, the independence of data from the observation should be maximized as a general principle. The "third-person" perspective in science as being the most "impartial" perspective became standard, because minimizes bias while also allowing for replication of results. I don't see any controversy about that. Nonetheless, none of these philosophical historical contexts were mentioned in the manuscript.

2. *"In contrast to other systems in the body, nervous system functions are unique in that all the higher brain functions are first-person properties of the mind."* Not true. There is a whole group of allocentric systems in the brain, the hippocampus and a number of temporal lobe areas.
3. Extract from Introduction: *"First-person reports of these sensations through motor activity such as behaviour and speech provide surrogate markers to the third-person observers. Currently, clinical evaluation of neurological and psychiatric diseases is based on assessing the first-person reporting and third-person observed findings. This severely limits our understanding of a) internal sensations in non-responsive patients, b) defects in the mechanism of formation of the internal sensation of memory, and c) the compelling sense of reality of hallucinations in psychiatric disorders."* These are not factors that inherently limit our understanding. We all know what hallucinations mean. Mentally healthy people are able to communicate with a certain degree of clarity their internal states and the listeners are able to relate to them. The locked-in syndrome is a different issue, which requires special methods to establish communication. We are also able to communicate our introspection by descriptions. For example, pain scales, memory tests, and tests of awareness are widely used in clinical practice. In contrast there is a much bigger communication barrier between animal species and humans preventing from obtaining first-person accounts that IS an inherent limitation of interpreting data from animal models, such as "fear" and "anxiety" for example. Because the motivation of the whole paper hinges on the quoted arguments and they are weak, they are unable to support the rest of the paper.
4. Notably, first-person reports are not at all alien to science. Sigmund Freud's legacy and specifically the psychoanalytic method are fundamentally based on first-person reporting and reference for interpretation. A method, which is often criticized (see for instance by Karl Popper) as lacking of scientific rigor, and more so because of the psychoanalytic reasoning is theoretically unfalsifiable. Other methods of self reports and introspection were always part of scientific resources, from the ancient Greek thinkers to contemporary psychophysics and still are important components of clinical case studies. Nevertheless, consolidation of first-person ontology with third-person objectivity have been initiated by a number of scholars, for example Francisco Varela (Shear and Jonathan 1999), Josephson (Josephson 1996), and Daniel Dennett in his Heterophenomenology (D. C. Dennett 2001). Dennett noted: *"heterophenomenology is nothing new; it is nothing other than the method that has been used by psychophysicists, cognitive psychologists, clinical neuropsychologists, and just about everybody who has ever purported to study human consciousness in a serious, scientific way."* (D. C. (. C. Dennett 1991). Moreover, Dennett writes in Consciousness Explained, *"I described a method, heterophenomenology, which was explicitly designed to be the neutral path leading from objective physical science and its insistence on the third-person point of view, to a method of phenomenological description that can (in principle) do justice to the most private and ineffable subjective experiences, while never abandoning the methodological principles of science."* (CE,

p72.)

5. Still in Introduction: "..., almost all the current approaches use third-person observed findings at various levels⁴ in correlational studies with surrogate makers of biochemical changes, neuronal activations, oscillating potentials, signal changes in imaging studies, and behavioural responses to connect with the first-person properties." Not at all. A number of those changes (biochemical changes, neuronal activation, oscillating potentials) never reach first-person quality and remain unconscious to the agent. Nobody feels the activity of a place cell firing in his/her hippocampus. Nevertheless, we know where we are at in an environment. The electrophysiological and neurochemical processes underlying the creation of representations and their readouts that may generate a first-person ontology are different entities, which are confused here.
6. "Emergence can be adopted as a framework to study properties that cannot be explained using the third-person-observed features of the system." Again, "emergence", a subject of a number of scientific investigations, one for instance in nonlinear dynamics, provided numerous insights and rigorous formalism, which comply well with third-person ("agent agnostic") observations.
7. In "Converting first-person sensations to third-person features". Quoting: "Recent research work is attempting to overcome this barrier by approaching higher brain functions from a first-person frame of reference" is a misrepresentation. A number of disciplines with long established history are devoted to study first-person frame of references. Classical psychophysics, research on episodic memories, consciousness, neuroeconomics, studies of decision-making and consumer behavior are all rely on first-person perspectives and first-person reporting.

After I argued that there is nothing new about first-person methods, I turn to the second aspect, the ontology of first-person reference.

B) First-person ontology

1. The separation and integration of first-person and third-person experience in a single brain derives from the duality of two systems: an allocentric (hippocampus) and egocentric system (parietal/occipital lobe/basal ganglia). The integration of information deriving from these two systems inside the brain is an intriguing question and a subject of active research. Nevertheless, according to a common working hypothesis, the third-person (allocentric reference) derives from the first-person (egocentric reference) experience. Hence the challenge is not how to explain the first-person experience, since sensory input is genuinely addressed in a first-person coordinates, but rather how does the brain arrive to the third-person (allocentric) representations from the first-person data. To bring an even more banal example, autonomous cars today use a navigation system, which converts first-person referenced information through cameras and the car's radar system to third-person information (map, distances of objects, movement of other objects on the map) and then converts it back to first-person instructions to change the speed and direction of the vehicle. No magic, no emergence, no need to change strategy in science just straightforward yet brilliant engineering.
2. "Focal points of emergence" this chapter is eluding to the idea that dendritic spikes are utilized to form sources of first-person ontology. The assumption that subthreshold

postsynaptic activity does not have a contribution to the neuronal signal processing is incorrect. Although these subthreshold events may fail to elicit action potentials (by definition), their contribution to the membrane potential oscillation that affects the integration of subsequent EPSPs in the same neuron is undeniable. Therefore, these subthreshold events are not merely a waste of energy waiting for a function to support. Even if their role is still elusive, nothing implies that they play a specific role in conveying "first-person" modality of information. Hence the answer to the question *"At what focal points in the nervous system do the units of internal sensations emerge?"* does not make sense, because *"internal sensations"* are unlikely to be caused by mechanisms different from external sensations, but instead they are pathway dependent.

3. Moreover, the same question *"At what focal points in the nervous system do the units of internal sensations emerge?"* implies yet another confusion. "Internal sensations" and first-person ontology are not the same. "Internal sensation" is not a term, introduced by the author's earlier paper (*"The nature of 'internal sensations' of higher brain functions may be derived from the design rules for artificial machines that can produce them"* (Vadakkan 2012)). The closest interpretation of it is "interoception", which are sensations deriving from inside the body. However, based on the context the author uses *"internal sensation"* as a sensory stimulus with a first-person quality. Most sensory, except interoception, are reporting third-person qualities. A color of an object in my visual field is rarely interpreted as first-person experience, it is a feature attributed to an object, regardless I am looking at the object or I am not. When the first-person quality of sensory input is concerned, arguably, conscious perception emerges at the level between the primary and secondary sensory cortical areas in the mammalian brain. The exact location and mechanism of the "conscious quality" are still argued (Koch 2004).
4. Even though our consciousness has a first-person ontology, not all higher brain functions are first-person experiences. To give a few examples, declarative memory is lacking first-person ontology. Also, hippocampus-dependent spatial memory transforms egocentric sensory information into allocentric or object-centered coordinate systems. Following up on the dorsal visual stream, we see the sensory information progressively being transformed to an allocentric coordinate system as information become increasingly independent of the sensory data source and also invariant of the position of sensory data acquisition. Hence, higher brain functions do not require first-person perspective.
5. Because first person experiences are phenomenologically inaccessible without making them third-person experiences, they can only be simulated by another person. Simulation, however, does not equal understanding. Conveying first-person experiences is not necessarily the function of science. It is more suitable to Art. The systematic studying of the origin of first-person experience is the subject of *consciousness* research and it is referred as the "hard-problem" of consciousness (Chalmers 1995) or *"Qualia"*. The history of psychology and neuroscience provides great examples such as the **Weber-Fechner's law** (and related Stevens' power law) how physical magnitude of the stimulus translates to sensation. The law will never reproduce the sensation but describes the phenomenon. Next is *"The first step is the theoretical derivation of the basic functional units of the system at the correct level that is also connected to the motor system, which can explain all the higher brain functions along with behavioral motor activity."* This is also called modeling. Indeed, since Turing, our proof of understanding relies on conceptual or quantitative or physical realization of models. Again,

nothing new is here. In summary, the description of first-person experience in Neuroscience is only relevant when addressing consciousness and methodology follows the same as any other subject, modeling and reverse engineering (see next).

6. *"The Gold Standard"*: I don't see any innovative approach here. We neuroscientists consciously or by intuition follow Allan Turing's legacy and method of understanding brain functions in terms of modeling them by machines that are able to reproduce those functions and essentially capable of learning from experience. Such an autonomous systems at certain point *may* generate internal representations that *may have* a first-person quality as it achieves the capacity of detaching itself from the observed world (have a concept of 'self') and also able to correctly reference (localize) those representations as its own (the Cartesian criterion of consciousness).
7. *"Major Hurdles"*: The statements *"Since the mechanism of the nervous system functions has not discovered yet, it is understandable that a novel approach is required"* is overly general and meaningless. It does not imply the next sentence: *"Changing the frame of reference from which to examine the higher brain functions suits such an anticipation."* Why would changing of the reference suddenly explain the function of the nervous system, if that was not obvious from an objective (third-person) point of reference?
8. The *"fear of discovering the operations of the mind"* and the *"growing concern about 'the Singularity'"* are popular concepts that are fun to entertain, but lacking substance. If I can afford a "first-person" comment, in light of recent political events, we seem to way overestimate the collective human intelligence, which is unable to cope with burning issues such as social injustice and terrorism, religious fanaticism, global environmental catastrophe, etc., relative to which the fear of AI turning against humanity is irrelevant. Humanity needs to defend itself from itself.
9. In the *"In Conclusions"* section the author lists a bunch of disconnected ideas such as *"low-level species produce intentionality to carry out survival and reproductive instincts"* and *"[first-person intelligent systems will] provide methods to prevent climate change"* and *"first-person properties will have similarities to the development of complex numbers in mathematics"*. These predictions are overly ambitious and unsubstantiated while also lacking any references.
10. First-person view is also an interpreted view as much as third-person referenced information. Every measurement is affected by the imprecision of the measuring device. Take for an example sensory transmission. The brain has to compensate for the delay of the information transfer, such as conduction delays relative to the onset of events. Libet showed that this indeed the case and introduced the term of *"subjective referral"* (Libet *et al.* 1979). Hence, not even the first-person point of view is reliable. We needed a third-person point of view (the observer reading the clock in Libet's experiment) to show its imprecision. The notion raises a question, isn't the first-person point of view just a construct? If it is, then how is it different from a third-person reference?
11. I return to the question again: How would it help to have first-person point of view? What problem would it solve that **could not be solved by third-person point of view**?
12. Lastly, the author fails to give us an example for what information may first-person reference provide that the third-person reference cannot. I do not see any symmetry

breaking between first-person vs. third-person reference frames. Since we are sharing the same universe instead of each of us encompassing his/her own private universe, using an outside reference is more parsimonious than taking only a first-person perspectives.

While the question of how the brain acquires first-person view remains to be a challenging one (not the subject of this manuscript), the author failed to convince the reader that methods of studying the underlying mechanisms need a fundamental revision. If I seriously misunderstood the author's position, I am open to follow up on a discussion and revise my opinion.

In summary, the first-person frame of reference is not novel, and the article fails to provide examples of new insights deriving from this approach.

Last remark: If the author claims that both point of views are useful for grasping the complexity and multifaceted human mind I must agree, however it is not clear whether the author suggests to switch completely to the first-person reference frame.

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Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 11 Jan 2017

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I thank Dr. Zoltan Nadasdy for his comments.

I understand that I didn't provide the logical arguments well in the initial manuscript. Explaining the need for a frame change made it difficult. I have rewritten the article to

explain the necessity for examining the system from a first-person frame of reference. I have provided additional references to the first-person methods of previous investigators.

I find that there was a confusion between a) the work by previous investigators who used first-person reporting of the inner sensations and b) the subject of the present work that explains the need for making a first-person approach to understand the mechanism of generation of first-person inner sensations. The first-person methods used in the past relied on behavioral expression of the contents of the inner sensations in the form of language. The results of those approaches have not helped us to derive a cellular level mechanism that generates the first-person inner sensations for solving the system. I have explained why the observer has to undertake an examination from the first-person frame of reference at the cellular-level to derive the qualia of the sensory content of the internal sensations.

The first-person inner sensations of different higher brain functions such as perception and memory are not accessible by third-person approaches, making it difficult to understand the operations of the nervous system. The seriousness of this will become very clear when we keep a gold standard of replication of the mechanism in an engineered system as the criteria for understanding the system. It can be initiated by asking the question "What properties should be present in a synaptically-connected nervous system to generate internal sensations when replicated in an engineered system?" This immediately provokes one to examine the system operations for the locations, systems conditions and mechanism for the generation of internal sensations.

It is expected that learning induces signature changes from which internal sensations are generated. By keeping all the constraints, a search for the locations and the conditions where the cue stimulus can induce internal sensations can be carried out. Under appropriate conditions, the mechanism at an optimal location is expected to make an approach "from within" the system to sense the qualia of the retrieved memories. This is expected to involve a retrograde search from the optimal locations towards the sensory receptors for sensing the sensory stimuli that can activate those receptors. In other words, the cue stimulus reaches at the locations where learning has made changes and reactivates the system to make a first-person approach towards the sensory receptor level to sense the sensory qualities of the stimuli required to activate those receptors. The observer who would like to trace the above path has to follow the same path, which will constitute the examination from a first-person frame of reference. No previous first-person studies have undertaken this novel approach.

I have kept strict criteria for the verification of the above mechanism by adhering to the acceptable scientific standards. The derived mechanism should be able to make predictions that can be verified. Different nervous systems can be examined for comparable circuitries. By keeping the gold standard of replicating the mechanism in engineered systems, the investigations can focus directly on the problem.

As the reviewer pointed out, current measurements in physics are being carried out without taking into account the observing subject. Both Ervin Schrödinger and Niels Bohr knew about it very well and they have mentioned it in their papers (1, 2). Recent attempts to incorporate the subject in the measurements (3) is a clear example of the need for

understanding perception. In this context, knowing how the nervous system is making subjective assessment through the formation of first-person inner sensations is of great importance.

The division of the human brain functions into allocentric and egocentric was made at a time when only one option of third-person observations was available. The current work introduces the option to make a first-person examination of the system for its operations. In this context, we need to take a fresh look at the system. Once the basic principle is discovered, the reasons for differences in the function at different locations can be determined. For example, the hippocampus has new granule neuron formation, which will continuously alter the circuitry at the higher neuronal orders above the level of the granule neurons. The effect of this on the first-person qualia generated at specific locations in the brain circuitry can be examined for details.

Reviewer has pointed out that my opinion article has concluded that the current methods of studying the underlying mechanisms need a fundamental revision. Even though, I want to remain modest, I would like to face the reality. The severe difficulties for discovering how first-person properties are generated within the system indicates that some major revision will be required at some level to find the solution. Large amount of data has already been collected by examining different nervous systems from different levels. This will allow for rigorous testing of any newly derived operational mechanism.

I have to admit that both the third-person observations and examination from the first-person frame of reference are required for grasping the human mind. For instance, this opinion article has used third-person observations made by investigators from a large number of laboratories to derive a feasible mechanism for the generation of first-person inner sensations. However, examination of the system from a first-person frame of reference will be a necessary step at some point during the investigation.

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Competing Interests: U.S. patent number 9477924 pertains to an electronic circuit model of the inter-postsynaptic functional LINK.

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Xiao Shifu

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This article impressed me. I personally respect the thinking of the author on researches. Referring to mathematics, neuroscience, the systems science, biological systems, evolutionary biology, comparative physiology and artificial intelligence, the author has an open mind and provides us a possible direction and approach to study higher brain functions. Meanwhile I have some different ideas, and I hope the author could consider these:

1. In the introduction section, you have introduced a lot for us, but could you tell us more clearly what's 'the necessity of studying higher brain functions from a first-person frame of reference'?
2. About the clinical approach we use now, the limitation you described in this article does not only exist in this approach, it exists on every approach because researchers haven't found out the mechanism of formation of internal sensations.
3. I can't understand these sentences you said in this article: 'It is found that a) locations from which memories can be retrieved gradually shift from the hippocampus to the cortices over several years, and **b) patients recover completely after suffering from small strokes at certain locations of the brain**'. These suggest that the basic structure-function units are spatially defiable and transferable, and that emergent functions can be integrated from multiple locations', please tell us how you draw your conclusion from this.
4. Could you tell us further information about the relationship between 'structure-function units' and 'views of emergent properties and reductionism', so we can get a clearer impression, even it's just an assumption.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 11 Jan 2017

Kunjumon Vadakkan, University of Toronto, Toronto, Canada

I thank Dr. Xiao Shifu for his comments and helpful suggestions.

I have removed sentences that were causing confusion. I have re-written the article to explain clearly why it is necessary to study the higher brain functions from a first-person

frame of reference. I sincerely hope that this revised manuscript provides necessary explanations.

Competing Interests: U.S. patent number 9477924 pertains to an electronic circuit model of the inter-postsynaptic functional LINK.

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