OPINION ARTICLE

On the primacy and irreducible nature of first-person versus third-person information [version 1; peer review: 2 approved with reservations]

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Abstract

In this essay, we will support the claim that a) some first-person accounts cannot be reduced to their third-person neural and psychophysiological correlates and b) that these first-person accounts are the only information to reckon when it is necessary to analyse qualia contents.

Consequently, for many phenomena, first-person accounts are the only reliable source of information available and the knowledge of their neural and psychophysical correlates don't offer any additional information about them.

Keywords

first-person, third-person, consciousness, mind-brain relationship

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Introduction

First-person accounts (IPAs) are written, verbal or intentional (conscious) behaviour, e.g. sign language, accounts related to what a person feels, perceives or thinks, in other words, every mental content the person is aware of and can communicate to others if requested or desired. “*I feel happy today*”; “*I see a pink rose*”; “*This panorama is awesome*”; and “*I think I had better do it tomorrow*”, etc. are some typical examples.

On the contrary, third-person accounts (3PAs), are identical types of accounts plus their neuro and psychophysiological correlates, obtained by people who observe or measure other behaviour and mental contents and processes. “*He seems happy*”; “*She’s looking at a rose*”, and “*He pushed the red button*”, are example of verbal accounts. “*The power of his EEG alpha band had an increase of 10%, when he relaxed*”; “*The medial frontal cortex increased its activity when she smiled at her partner*”, and “*Her heart rate decreased from 80 bpm to 60 bpm, when she heard pleasant music*”, are examples of neuro and psychophysiological correlates of mental activity of the observed person.

In this essay, we will support the claim that a) some IPAs cannot be reduced to third-person neural and psychophysiological correlates accounts (3PAs) (We will not enter here in the debate about how IPAs can also considered 3PAs (Piccinini, 2010) with particular reference to the heterophenomenology as defined by Dennett (2003) and b) that their contents are the only information to reckon when it is necessary to analyse qualia contents, that is, emotions, beliefs, reality interpretations, quality of life and health and their effects on behaviour and the brain activity. Consequently, c) even a complete description of the brain and psychophysiological correlates of these IPAs does not add any further information about their contents and characteristics.

This approach is at odds with the view that given the subjective and introspective nature of IPAs, they lack objective contents and hence 3PAs are undeniably more informative.

There is not space here to describe the historical reasons of why, in psychology, IPAs lost their importance in comparison to 3PAs. For those readers interested in this topic we suggest to refer to Klein (2015b).

When first-person accounts are not reliable

Since the seminal paper of Nisbett & Wilson (1977) evidence has been accumulated showing that people IPAs can fail in the detection of their decision processes (but see Pettimengin et al., 2013, for a manipulation which reverted the accuracy to an high level).

According to Schooler (2015), IPAs become unreliable when translation dissociations occur. Translation dissociations “*correspond to situations in which, while in the process of re-representation, one omits, distorts, or otherwise misrepresents one’s mental state to oneself and/or others.*”page 9.

A typical example is the monitoring of mind-wandering which is typically measured using self-catching and experience sampling techniques. Self-catching asks participants to monitor their mental activity and signal, for example by pressing a button, when they notice their mind activity was off-task. With experience sampling techniques, participants are probed to notice whether their mind was wandering at random time intervals.

When first-person accounts are the only valid information to consider

Below is a (non-exhaustive) list of phenomena and conditions that can be described and known only by IPAs whereas the third-person correlates are irrelevant in order to understand their characteristics. For each of the selected phenomena we will present some examples of IPAs and 3PAs to make evident the different informational value of these accounts as supportive of our main thesis.

Sensations and Emotions

Emotions and Emotion (Mood) Disorders. Emotions identification and their valence and arousal can be measured only taking in account IPAs. For example the Self-Assessment Manikin in different version, see Figure 1 as an example, was used for the database of the International Affective Pictures System, whereas bipolar semantic slider scales from from 1 to 9, were used for the Nencki Affective Picture System (Marchewka et al., 2014)

As for the measure of emotions triggered by pictures, faces, persons, etc., even the measure of the mood and its disorders can only be done by referring to IPAs, usually by way of structured questionnaires, e.g. the Beck Depression Inventory or interviews, e.g. The Structured Clinical Interview for DSM-5 (SCID-5), in which participants respond with their extent of agreement with statements such as “*I feel sad*” or “*I don’t cry any more than usual*”, etc.

On the contrary, neuro and psychophysiological accounts (e.g. Allen et al., 2004; Lin et al., 2010), consists of biological signals that cannot convey any subjective and qualitative information about their contents but simply represent a correlation with a different type of information. For example Matsubara et al. (2016), found that the anterior cingulate cortex volume could be a distinct endophenotype of bipolar disorders, while the insular volume could be a shared bipolar disorders and major depressive disorder endophenotype. Moreover, the insula could be associated with cognitive decline and poor outcome in bipolar disorders. Can we use this information to integrate our knowledge about the characteristics of bipolar and depressive disorders of those participants?

Pain

Visual analogue, numerical rating and verbal rating scales (see Figure 2) are commonly used to assess pain intensity in clinical trials and in other types of studies. Among the multidimensional questionnaires designed to assess pain, the McGill Pain Questionnaire and Brief Pain Inventory are valid in many multilingual versions (Caraceni et al., 2002).

Figure 1. An example of the Self-Assessment Manikin for the measure of emotions' characteristics. In this case the participant is requested to rate the emotional valence and arousal of a stimulus on a 5-point scale. This figure has been reproduced with permission from Li *et al.*, 2011.

Figure 2. Example of a visual analog scale to measure pain. Participants are requested to rate their perceived pain choosing one of the six different options. No copyrighted figure.

An example of a 3PAs account is “The insula ipsilateral to the site of needling was activated to a greater extent during real acupuncture than during the placebo intervention” (Pariente *et al.*, 2005). It seems clear that this type of information cannot convey any useful information about the subjective quality of pain of the persons experiencing it.

Conscious experiences

Anomalous or non-ordinary experiences

Anomalous or non-ordinary experiences comprise a large group of personal experiences characterized by the lack of any clinical psychopathological syndrome, even if they may appear associated with some of them (Cardena & Facco, 2015; Cardena *et al.*, 2014).

Among these experiences there are:

Spiritual experiences. Spiritual experiences, independently from how they are obtained, e.g. spiritual practices, e.g. meditation (Chen *et al.*, 2011), spontaneously or by using psychotropic drugs like the psilocybin (Griffiths *et al.*, 2008), are only based on 1PAs.

The Revised Mystical Experience Questionnaire (Barrett *et al.*, 2015) is one of the available questionnaires for the investigation of these experiences. Participants are requested to express their degree of experience related, for example to: loss of usual sense of time; experience of amazement; sense that the experience cannot be described adequately in words; gain of insightful knowledge experienced at an intuitive level, etc.

Beauregard & Paquette (2006), investigated the neural correlates of such a type of experiences in a group of Carmelite nuns and found that this state was associated with significant loci of activation in the right medial orbitofrontal cortex, right middle temporal cortex, right inferior and superior parietal lobules, right caudate, left medial prefrontal cortex, left anterior cingulate cortex, left inferior parietal lobule, left insula, left caudate, and left brainstem. Can we achieve better understanding of the quality of these experiences with this information?

Near-Death-Experiences. Near-Death-Experiences are peculiar mental experiences reported by persons who suffered severe injuries, e.g. cardiac arrest (Agrillo, 2011; Facco & Agrillo, 2012; van Lommel, 2011), characterized by increased vividness and sense of reality with respect to the normal awake state when neither consciousness nor cortical activity is expected: e.g. “Super awake. I could sense things more than I do in my usual state of awareness”, plus other peculiar experiences, for example encounters with spiritual beings: e.g. “I do remember a being of light, God, standing near me” and experiences of living a timeless dimension: e.g. “I became time and space”, etc. (Excerpts from the <http://www.nderf.org/Archives/exceptional.html> database)

Mobbs & Watt, (2011) are among those who are trying to explain these experiences as simply epiphenomena of some neural activity. For example, they stated: “the vivid pleasure frequently experienced in near-death experiences may be the result of fear-elicited opioid release, while the life review and REM components of the near-death experience could be attributed to the action of the locus coeruleus- noradrenaline system”(page 449). However statements like these, take for granted that the neural correlates “translate” into subjective experiences forgetting to offer a testable hypothesis on how this transformation can take place. Furthermore, this hypothesis of opioids has several weaknesses (Ersek *et al.*, 2004; Facco, 2010; Facco & Agrillo, 2012; Lawlor & Bruera, 2002; Vella-Brincat & Macleod, 2007), that is: a) opioids are only wake hallucinogens, b) people administered opioids for pain therapy do not experience NDEs, while their adverse events may include a delirium, the phenomenology of which is totally different with from NDEs; c) No hallucinogens induce standard reproducible experiences, which largely depend on subjects’ personalities, aims of their intake, context and ritual. In other words, when new facts challenge the endorsed axioms and theories, they are first interpreted trying to constraint them within the available knowledge,

while their explanation may call for new, yet unknown, laws of nature (i.e., properties of consciousness).

Memory

Differently from implicit memory, e.g. procedural and associative memory, all aspects of explicit memory, e.g. autobiographical, semantic, have to rely only on 1PAs (Wilson, 2002). For example, testing autobiographical memory requires the participants to retrieve and describe personal life episodes, e.g. celebrations, diseases, special encounters with friends and relatives, etc.

Moreover Klein (2015) extensively discussed that in order to qualify as memory, “the product of learning needs to be a mental state that includes the feeling that one is reliving a past experience—that is, it provides a directly-given, non-inferential sense that one’s current mental state reflects a happening from one’s past.” (page 2). This distinction allows to interpret a series of impairments characterized by a dissociation between memory contents and the feeling of ownership of them (Klein, 2015a)

As to an example of 3PAs, Conway *et al.* (2001), recording the slow cortical potentials, found that left frontal negativity primarily reflects cortical activation associated with the operation of a complex retrieval process, whereas the later temporal and occipital negativity (the result of the retrieval process) reflects activation corresponding to the formation and maintenance of a detailed memory. Can you extract useful information related to the contents and the subjective experience of memory of participants from these data?

Reasoning

Among the many tasks that can be used to investigate reasoning, one is to judge whether the final statement after a series of propositions is true or false. For example, “All men are animals. All animals are mortal. Hence, all men are mortal.”: True or False?. Papageorgiou *et al.* (2016), investigated the EEG correlates of a series of valid and paradoxical statements and found that “During the processing of paradoxes, results demonstrated a more positive event-related potential deflection (P300) across frontal regions, whereas processing of valid statements was associated with noticeable P300 amplitudes across parieto-occipital regions”. Is there any useful information in these data that can integrate what the participants experience as thoughts, feelings and emotions?

Furthermore, any judgement in terms of true vs false, is closely dependent on culture and available knowledge and, thus, is intrinsically weak and provisional. Judgements on both truth and falsity as well as paradoxes may change over time: for example the unity of space-time and matter-energy, the Heisenberg’s principle of indetermination and the concept of entanglement look to be true in quantum physics, false or ununderstandable according to classical, Newtonian physics. Thus, neurophysiological data about judgements can only provide an estimation of brain mechanisms and, at best, helping one to check whether the subject is processing them as paradoxes or valid statements, without any possible inference on subject’s experience, cultural components and, last but not least, on knowledge and comprehension of the truth, which remains in the realm of mind.

Beliefs and Self-evaluations

Beliefs and delusional beliefs

All cultural, ethical, religious, cultural and scientific beliefs as well as all kinds of delusional beliefs, can only be known by using IPAs (e.g. Coltheart *et al.*, 2011; Jonas & Fischer, 2006; Zeidler *et al.*, 2002).

For example, Kapogiannis *et al.* (2009), investigated the neural correlates of three psychological dimensions of religious belief (God's perceived level of involvement, God's perceived emotion, and doctrinal/experiential religious knowledge). Participants IPAs were obtained by requesting to rate different statements, e.g. "God cares about the worlds' welfare"; "All religions have truth", on a 7-point Likert scale. The neural correlates of these dimensions were investigated by using fMRI. These authors found different neural networks associated with the three religious beliefs, e.g. more activation of bilateral inferior frontal gyrus, pars triangularis and Brodman area 45 in relationship with God's lack of involvement and more activation of the right middle frontal gyrus and Brodman area 11 in relationship to statements reflecting God's love etc.

How much information can we add to what we obtained from IPAs by using these 3PAs?

Hallucinations

Visual and auditory hallucinations such as hearing voices (Holt & Tickle, 2014), can be identified and assessed by using IPAs (Haddock *et al.*, 1999).

Barkus *et al.* (2007), investigating the neural correlates of non-clinical auditory hallucinations of a group of participants by using the fMRI, found increased activation in the superior and middle temporal cortex. Does this information helped to increase what authors already knew about the auditory hallucinations of their participants?

Placebo

The core components of placebo and nocebo effects are expectations/beliefs and conditioned reactions (Price *et al.*, 2008; Rief & Petrie, 2016). Whereas conditioned reactions can be activated bypassing any mental activity, expectations and beliefs are intrinsically IPAs independently from whether people are aware or not of them (Jensen *et al.*, 2012) and cannot be interpretable by using their neural correlates.

Risk perception

Risk perception both for natural, economic, political and hazard events is another important mental content that can only measured by using IPAs (Sjoberg, 2000).

For example, Schmälzle *et al.* (2011), investigated the HIV risk perception by presenting photographs of unknown persons and recording the EEG evoked response potentials.

They found that the implicit processing of individuals prone to risky behavior was associated with an early occipital negativity

(240–300 ms) and a subsequent central positivity between 430 and 530 ms compared to individuals with safer practices. It appears evident that this information cannot be used to increase the knowledge about risk perception obtained by IPAs.

Aesthetic appreciation and judgments

All natural (Daniel & Meitner, 2001), human (Berggren *et al.*, 2010), animal and aesthetic appreciation and judgments, can only be assessed by IPAs (Leder *et al.*, 2004).

Thakral *et al.* (2012), investigated the neural correlates of van Gogh paintings evoking a range of motion experience by using the fMRI and found that the sensory motion processing region MT+ activity was correlated to the degree of motion experience (but not the experience of pleasantness), whereas the experience of pleasantness (but not motion experience) was associated with an increased activity in the right anterior prefrontal cortex. Can this neural information add any useful information about pleasantness and motion appreciation experienced by these participants?

Quality of life and health

The World Health Organisation (WHO) define quality of life (QoL) as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHO, 1998). QoL is evaluated by different versions of questionnaire of which the best known are those developed by the WHOQOL groups (WHO, 1998; WHOQOL Group, 1995).

Urry *et al.* (2004) requested their participants to complete self-report measures of eudaimonic (leading a virtuous life and doing what is worth doing) well-being, hedonic well-being, and positive affect and subsequently recorded their EEG activity. They found a greater left than right superior frontal activation association with higher levels of both forms of well-being. May we use this information to gather more details about what already participants reported in their IPAs?

Discussion

As anticipated in the introduction, the aim of this essay was that of supporting the claim that there are many varieties of IPAs the contents and characteristics of which can be known and investigated only by these accounts and cannot be integrated with information gathered by 3PAs in particular those related to their neural or psychophysiological correlates.

We have listed ten types of phenomena that can be studied only by referring to IPAs, even if for each of them there is a legitimate interest in knowing their neural and psychophysiological correlates. However it is important to realize, on the part of both researchers and the funders of their investigations, that the knowledge of their neural and psychophysiological correlates has nothing to add to the knowledge of these phenomena.

According to the authors of "Neuromania: on the limits of brain science" (Legrenzi & Umiltà, 2011) the popularity of the prefix "neuro" before economy (Camerer *et al.*, 2005), aesthetics

(Skov & Vartanian, 2009), marketing (Ariely & Berns, 2010), theology (Barrett, 2011), etc., represents a degeneration of an acritical adhesion of a metaphysical physicalism or mind-brain identity theory and of a superficial knowledge of the complex relationship between mind contents and its neural correlates. Many authors continue to alert researchers about the problems in defining such relationship. Max Coltheart for example repeatedly warned that “testing theories of cognition” by using fMRI investigations requires “both sensitivity (a claim that brain region *X* will always be active when cognitive process *C* is being executed) and specificity (the claim that brain region *X* will not be active except when cognitive process *C* is being executed), pag.102 (Coltheart, 2013) avoiding the so-called “consistency fallacy” that is the erroneous inference that when data that are consistent with some theory they cannot, just in virtue of this consistency, be offered as the only evidence in support of that theory. Something additional is needed, that is, evidence against the contradictory of the hypothesis.

Our statement that IPAs are irriducible to 3PAs, could be falsified by the evidence suggesting that it is possible to change IPAs by acting on their biological correlates. For example Saitoh *et al.* (2007) were successful in reducing pain due to spinal cord or peripheral lesions by applying high-frequency repetitive transcranial magnetic stimulation on the primary motor cortex. Conversely, hypnosis may yield a significant increase of pain threshold up to the level of surgical anesthesia: providing proper instructions and suggestions to the patient (Facco *et al.*, 2011; Facco *et al.*, 2013); this is a very relevant fact allowing for Enhanced Recovery After Surgery without costs and adverse events (Facco, 2016); the same is for meditation a valuable introspective technique sharing several features with hypnosis (Facco, 2017). As a result, the IPA is no less relevant than 3PA, even in the context of the pragmatic approach of clinical medicine, despite having been understated by the ruling reductionist paradigm.

The main aim of our paper is not that of supporting the view that the study of the biological correlates of many IPAs is irrelevant and a waste of resources, but that the information we can gather from IPAs are irriducible to 3PAs and these cannot increase the information we got from IPAs even when is it possible to infer a direct causal relationship between 3PAs and IPAs. In fact in the Saitoh *et al.* (2007) example, the modification of primary cortex activity do not contain any useful information about the participants' change in pain perception.

Our approach is akin Jack's (2013) statements “.. our experiential understanding of our own minds is fundamentally different from, and at least to some degree incompatible with, our understanding of the mind as a mechanism. At the same time, this experiential understanding is no less important than our mechanistic understanding of the mind. In fact, it is more important. Our experiential perspective guides our understanding of ourselves, and serves as the compass which aids our navigation through the social world, allowing us to see, and ultimately connect to, the humanity in others. page 670”.

Similar position is held by Guta, (2015): “..the knowledge [neural, chemical, electrical activities that take place in the brain] we gather in this regard, no matter how detailed it may turn out to be, offers no help whatsoever in and of itself by way of giving us access to the first-person data. To retrieve the latter data, the right thing to do would be to directly engage with subjects of experience, that is, with people. The imaging techniques scan brains but not people's thoughts/intentions/plans/regrets, and the list goes on and on. page 241”

We hope this essay will alert all scientists who are endorsing a metaphysical fisicalist approach who posit that all mind contents are nothing but a byproduct of the brain or emerging properties of its computational complexity (Schwartz *et al.*, 2016; Smart, 2014) that for many phenomena, the IPAs are the only reliable source of information available and that the knowledge of their neural and psychophysical correlates does not offer any additional information about them. Furthermore, the wealth of data available on hypnosis and meditation see (Facco, 2014; Facco, 2017), as well as music perception and performance (Fauvel *et al.*, 2014; Han *et al.*, 2009; Koelsch *et al.*, 2005; Ohnishi *et al.*, 2001) provide an increasing evidence that the mind-brain relationship is not an unidirectional one, defined by a bottom-up hierarchy from brain to mind; rather, it can be better conceived as a bidirectional relationship, where mind may also engender both functional and steady, structural changes in the brain. Needless to say, music, its value and meaning, can only exist in the realm of IPA. The whole problem is endowed with huge epistemological and metaphysical implications, to be reappraised in order to avoid any inadvertent dogmatic drift in the scientific approach to the world of subjectivity (Klein, 2013)

Given the enormous investments in the brain research both in the USA and Europe (see Global Brain Workshop, 2016; Markram, 2012), there is a serious risk that very few research resources (e.g. funds, personnel, etc.) will be devoted to the investigation of IPAs. It is curious that a similar worry is shared by supporters of a mind-brain fisicalist metaphysic like Schwartz *et al.*, (2016), when they declare that “..an eliminative reductionist perspective, in which behaviors, thoughts, feelings, and other experiences can be completely explained by biological processes at the cellular and molecular levels, may be difficult to square with much current scholarship in neuroscience and in the broader field of psychology. Nevertheless, given the dependence of researchers, departments, and universities on federal grant funding, priorities emphasized by funding agencies and by their review committees may “force the hands” of researchers, departments, and universities to prioritize neuroscience at the expense of other approaches”. Page 15

Following Stanley Klein discussion about the limitations of reducing the study of Psychological Science to its biological mechanisms, we endorse his claim that “experiential aspects of reality (reflected in mental construct terms such as memory, belief, thought, and desire) give us reason to remain open to the need for psychological explanation in the treatment of mind.” (Klein, 2016)

Author contributions

PT, EF and DL conceived the paper. PT and EF wrote it. All author were involved in its revision.

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Zoltan Kekecs

Lund University, Lund, Sweden

The authors present an opinion article summarizing information from prior literature in defence of their claims that a) some first-person accounts cannot be reduced to their third-person neural and psychophysiological correlates and b) that these first-person accounts are the only information to reckon when it is necessary to analyse qualia contents. I believe this is an important topic to discuss, even if I am sceptical about whether the issue underlying the arguments, the reducibility of qualia to psychophysiological information, is one that can be decided just through scientific insight. Nevertheless, I feel that the manuscript needs a thorough revision before being finalized, making the claims themselves and the logic of the arguments supporting them clearer.

The authors make several claims in this opinion article. One of the main points is summarized well in the Abstract and Discussion: "for many phenomena, first-person accounts are the only reliable source of information available and the knowledge of their neural and psychophysical correlates don't offer any additional information about them". Based on the information presented by the authors, I tend to agree with this statement if we start the sentence with "at this point in time" or "at our current level of scientific advancement".

It is true that presently our neuroimaging and electrophysiological monitoring techniques used in humans are extremely crude and come nowhere close to providing the level of detail that can be gained from a first person account on most of the listed phenomenon. However, the author's claim doesn't seem to stop at the present time. They seem to argue that third person accounts will never provide reliable information about the listed phenomena. This is problematic because this part of their claim is not justified by any arguments. Instead, the authors seem to extrapolate from the fact that third person accounts are unreliable today to the claim that they will always be unreliable and redundant compared to first person accounts. I think that this logical jump is too much to ask of the reader. Thus, either the claim should be restricted in time, or further argumentation is necessary.

Another issue with the manuscript in its current form is that 1PAs and subjective experiences (qualia), are often confused. For example in this sentence: "Our statement that 1PAs are

irreducible to 3PAs...". I like that the authors take the time to define both first person accounts and third person account in the beginning of the paper. However, the claim that 1PAs are irreducible to 3PAs are refuted by the very definition that the authors provide. 1PA is defined as: "First-person accounts (1PAs) are written, verbal or intentional (conscious) behaviour, e.g. sign language, accounts related to what a person feels, perceives or thinks, in other words, every mental content the person is aware of and can communicate to others if requested or desired." While 3PA is defined as: "third-person accounts (3PAs), are identical types of accounts plus their neuro and psychophysiological correlates, obtained by people who observe or measure other behaviour and mental contents and processes." An example for a 1PA by the authors is if a person says "I feel happy today". This accounts can always be directly transformed to a 3PA like: "She feels happy today". So in this sense a 1PA can be "reduced" or made directly equivalent to a 3PA.

At another point in the manuscript the authors use a longer version of this claim: "some 1PAs cannot be reduced to third-person neural and psychophysiological correlates accounts". However, this cannot be true either with the current definition the authors have for 1PA, because all of the examples the authors bring for 1PA can be reduced to muscle movement (speech, writing, sign language), and it is well established that muscle movements are directly evoked by neurobiological phenomenon. So it is logically possible to completely reduce the movements produced when a person utters "I have a throbbing pain in my temple" verbally or in sign language to its efferent neural source. In fact, we understand the processes that are at play here so well that we can create an artificial limb with which an arm amputee will become able to produce the same sign language sentence on her own again. So I would venture that reducing these reports themselves to their neurobiological correlates is not only a logical possibility, but is plausible within a few years of research.

I guess what the authors really meant is that the qualia, the subjective feeling of happiness or pain, the feeling that the 1PA refers to, can never be reduced to simple 3PAs (and because of the above argument about the equivalence of 1PAs and 3PAs, it cannot be reduced to 1PAs either if we define 1PAs as the authors do right now). So either the definition of 1PAs needs to be changed to involve the subjective feeling and not just the report of that feeling, or the manuscript needs to be looked over carefully to identify sections where the authors meant qualia (first person experiences) instead of first person reports about qualia.

I also feel that several statements and claims in the manuscript could be clarified. For example, the authors claim that "the knowledge of their neural and psychophysiological correlates has nothing to add to the knowledge of these phenomena". This statement is very general in its current form and the preceding text does not justify it. Let's take for example pain or mood disorders, example phenomena brought up by the authors. I believe we have gained extremely useful knowledge already about these phenomenon by understanding the neural and biochemical mechanisms involved in them, which help us in their respective treatment. We are able to further improve our treatments by understanding the mechanisms even better. I am sure that the authors did not mean that we cannot learn anything useful about these phenomenon by studying their neural correlates. They probably meant that we do not get any useful information on the exact quality of the subjective experiences involved in these phenomenon by studying their neuronal correlates, or something similar. If so, the original sentence needs much clarification.

The quote from Coltheart (2013) is also misleading: "testing theories of cognition" by using fMRI investigations requires "both sensitivity (a claim that brain region X will always be active when

cognitive process C is being executed) and specificity (the claim that brain region X will not be active except when cognitive process C is being executed).” I don’t think any brain researcher today would think that a certain area of the brain would be responsible for a single thought or idea and nothing else. This is not even true for individual neurons. It is the networks and connections that are proposed to do the computations, and a brain area and even individual neurons are suspected to be part of multiple networks. So in this sense we cannot and do not expect this kind of specificity of brain areas anymore.

It is strange that the authors bring up a fact that falsifies one of their claims and then they never explain why this falsification is invalid. It is left hanging in the air: “Our statement that 1PAs are irreducible to 3PAs, could be falsified by the evidence suggesting that it is possible to change 1PAs by acting on their biological correlates. For example Saitoh et al. (2007) were successful in reducing pain due to spinal cord or peripheral lesions by applying high-frequency repetitive transcranial magnetic stimulation on the primary motor cortex.” Later they add: “As a result, the 1PA is no less relevant than 3PA, even in the context of the pragmatic approach of clinical medicine, despite having been understated by the ruling reductionist paradigm.” However, this is nowhere near as strong a claim as the original one. The original claim is that 1PAs are irreducible to 3PAs, while the later claim is that 1PAs are relevant as well, not just 3PAs. By leaving the falsification open like this the authors practically invalidate one of their main claims in this opinion article, so it is strange why they make this claim the first place, if they think it is in fact false, or incomplete in its original form. I suggest either refuting the falsification, or elaborating their claim in its original form (at every instance of its appearance in the manuscript, not just after the falsification is mentioned in the end), so it is no longer falsified by the fact that it is possible to change 1PAs by acting on their biological correlates.

Relatedly, I found it unclear how does the fact that hypnosis brings about an increase in pain threshold relate to the same section. For me, this sentence in its context without any further explanation implied that the authors think that contrary to transcranial magnetic stimulation, hypnosis would affect 1PAs directly, without involving neural correlates of pain. This is not true, because we see from several neuroimaging studies that the brain behaves differently when noxious stimuli is applied with and without hypnosis. It is also very probable that hypnosis relies on at least some neural mechanisms to enact its effects on pain, if nothing else, by relying on the sensory neurons which allow the hypnosis participant to perceive the words of the hypnotherapist. If this sentence is important in the manuscript, the authors should make it clear how it is relevant exactly to this discussion. Otherwise I suggest deleting it because it invites misinterpretation.

It is also hard to see how does the following sentence help any of the arguments of the authors “In fact in the Saitoh et al. (2007) example, the modification of primary cortex activity do not contain any useful information about the participants’ change in pain perception.” Transcranial magnetic stimulation was an experimental manipulation in this example. I am not sure why should it contain any information on the change in pain perception. This is not a measurement, but a manipulation targeting the suspected mechanism underlying pain, which in the end was successfully able to modify the subjective pain experience, or at least the 1PA thereof. Similarly, a hammer blow does not have to contain information on the subjective quality of pain to cause pain. If the authors meant this sentence to refute the falsification, they need to make it clearer.

Correcting the following minor issues should also serve to improve the manuscript:

“opioids are only wake hallucinogens” – weak instead of wake

“according to classical, Newtonian physics” – according instead of according

“content that can only be measured by using 1PAs” – content that can only be measured by using 1PAs

Irreducible is spelled incorrectly as irriducible several times in the document

“this is a very relevant fact allowing for Enhanced Recovery After Surgery without costs” – why is Enhanced Recovery After Surgery capitalized? Furthermore, “without costs” indicates that this is a completely free intervention, however, most surgeries do not have a trained professional who can use hypnosis in a clinical setting, so in most cases this would require the presence of a new professional, who needs to be paid. And even if the medical staff gets the proper training, the training itself is not without costs, etc. So I suggest deleting “without costs” from this sentence.

Is the topic of the opinion article discussed accurately in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Are arguments sufficiently supported by evidence from the published literature?

No

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hypnosis, Psychophysiological mechanisms involved in mind-body interventions

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, however I have significant reservations, as outlined above.

Author Response 30 Apr 2017

Patrizio Tressoldi, Università di Padova, Padova, Italy

Thank you for your accurate and constructive review.

In the following, we will try to reply to all your main comments.

- “for many phenomena, first-person accounts are the only reliable source of information available and the knowledge of their neural and psychophysical correlates don’t offer any additional information about them”. Based on the information presented by the authors, I tend to agree with this statement if we start the sentence with “at this point in time” or “at our current level of scientific advancement”.

Reply: we added the sentence “at the current level of scientific advancement” both in the abstract and in the discussion.

- Another issue with the manuscript in its current form is that 1PAs and subjective experiences (qualia), are often confused.....An example for a 1PA by the authors is if a person says “I feel happy today”. This accounts can always be directly transformed to a 3PA like: “She feels happy today”. So in this sense a 1PA can be “reduced” or made directly equivalent to a 3PA.

Reply: even if in the paper we mainly referred to 3P neuro- and psychophysiological correlates, even the 3PA “*She feels happy today*” cannot convey any reliable information about how the person really feels happy. This 3PA remains an independent source of information and cannot guarantee what really the person feel. It is like to state “*Peter felt a strong pain after hammering his thumb*”, but only Peter can describe the degree and qualities of his pain.

- ...So either the definition of 1PAs needs to be changed to involve the subjective feeling and not just the report of that feeling,

Reply: in the Introduction we defined better our 1PA definition adding the term “qualia” with a reference.

- I am sure that the authors did not mean that we cannot learn anything useful about these phenomenon by studying their neural correlates. They probably meant that we do not get any useful information on the exact quality of the subjective experiences involved in these phenomenon by studying their neuronal correlates, or something similar.

Reply: This is precisely our core message. In fact, in the discussion we wrote “The main aim of our paper is not that of supporting the view that the study of the biological correlates of many 1PAs is irrelevant and a waste of resources, but that the information we can gather from 1PAs are irreducible to 3PAs and these ones cannot increase the information we got from 1PAs even when is it possible to infer a direct causal relationship between 3PAs and 1PAs.”

- The quote from Coltheart (2013) is also misleading:.... ‘I don’t think any brain researcher today would think that a certain area of the brain would be responsible for a single thought or idea and nothing else.

Reply: Coltheart’s et al. warnings are valid for any correlation between cognitive functions and their anatomical correlates independently if these ones are single or a network of brain areas. Unfortunately, these warnings are still largely ignored see for example. Tressoldi, P. E., Sella, F., Coltheart, M., & Umiltà, C. (2012). Using functional neuroimaging to test theories of cognition: A selective survey of studies from 2007 to 2011 as a contribution to the Decade of the Mind Initiative. *Cortex*, 48(9), 1247-1250.

- It is strange that the authors bring up a fact that falsifies one of their claims and then they never explain why this falsification is invalid I suggest either refuting the

falsification, or elaborating their claim in its original form (at every instance of its appearance in the manuscript, not just after the falsification is mentioned in the end), so it is no longer falsified by the fact that it is possible to change 1PAs by acting on their biological correlates.

Reply: we agree that the suggestion on how to falsify our main claim and the Saitoh example was badly presented. Now we revised that paragraph as follow: "Our statement that 1PAs are irreducible to 3PAs, could be falsified by the evidence that it is possible to determine precisely the changes and qualities of 1PAs only by observing the effects of the interventions on their biological correlates. For example, Saitoh et al. (2007) were successful in reducing pain due to spinal cord or peripheral lesions by applying high-frequency repetitive transcranial magnetic stimulation on the primary motor cortex. However, the modification of primary cortex activity didn't give any useful information about the participants' change in pain perception. In fact, this information was obtained by asking the participants to rate their pain with a visual analogue scale similar to that presented in Figure 2 and the Short-Form of the McGill Pain Questionnaire.

- .. the authors think that contrary to transcranial magnetic stimulation, hypnosis would affect 1PAs directly, without involving neural correlates of pain. This is not true,....

Reply: the example of hypnosis as a mean to influence pain perception has now be integrated with the Saitoh example: "Pain reduction can also be obtained by acting on mental beliefs and contents.....

Competing Interests: I'm the corresponding author

Reviewer Report 11 April 2017

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In the present opinion article ¹, the authors firstly present support for the claim that some first-person accounts (1PAs) cannot be reduced to third-person neural- and psychophysiological correlates accounts (3PAs). Secondly, they state that the 1PAs contents are the only information to

reckon when it is necessary to analyze qualia contents (e.g., emotions, beliefs, reality interpretations, quality of life and health) and their effects on behavior and the brain activity. Thirdly, according to the authors, even a complete description of the brain and psychophysiological correlates of these 1PAs does not add any further information about their contents and characteristics. Tressoldi *et al.* (2017) makes several challenging and highly interesting claims; moreover, they give a state of the art overview of the 1PAs and 3PAs results and research limitations so far. Last but not least, their article stimulates further discussion on how to best invest research money in order to make progress in this research field, all in all, we recommend publication, but we have several major and minor points that the authors should further address.

Firstly, the authors are right (see page 2) that 1PAs are useful in clinical research and diagnostics of psychiatric disorders because they provide subjective and qualitative information; however, on the other hand, we would like to stress that self-rating instruments, such as the Beck Depression Inventory-II (BDI-II)², have their own limitations³. For instance, the interpretation of results from self-report instruments in general but also for specific questionnaires, can contain flaws (e.g., Subjective Well-being under Neuroleptics scale – Short form, etc.)⁴. For instance, it was shown that patients might show a certain response pattern, like a tendency to exaggerate their symptoms or on the contrary, to willingly under-report the severity of their symptoms or the frequency in order to present their situation more positively³. In addition, test-taking attitude (e.g., social desirability) was found to play a critical role in the responses to clinical self-report instrument⁵. In other words, how should psychologists/psychiatrists deal with those methodological limitations in daily clinical practice according to the authors? In our opinion, relying on those (structured) questionnaire outcomes only, does not seem the way to go.

The authors are right when they write on page 3 about 3PAs: “It seems clear that this type of information cannot convey any useful information about the subjective quality of pain of the persons experiencing it”. However, the authors somehow do not mention that in the years after the Pariente *et al.* (2005)⁶ publication, the measurement of *deqi* scores of the participants in acupuncture studies were introduced and are now being collected alongside the 3PAs⁷⁻⁸, consisting of the following 12 *Deqi* sensations: aching, soreness, numbness, fullness, sharp or dull pain, pressure, heaviness, warmth, coolness, tingling, itching, and any others⁷⁻⁸. This methodology is also used in recent functional magnetic resonance imaging (fMRI) studies on acupuncture⁹; moreover, the MR signals of the brain areas that had been activated by acupuncture stimulation at a specific acupuncture point (for instance GB34) are then correlated⁹. The authors should add this to their manuscript because this would give a more complete picture of the current state of the art in this specific research field, especially since they attack this field for using 3PAs only, which is not correct.

Thirdly, one of their most provocative statements is the one on page 5 where the authors state: “However it is important to realize, on the part of both researchers and the funders of their investigations, that the knowledge of their neural and psychophysiological correlates *has nothing to add* to the knowledge of these phenomena”. We find this a challenging statement and we fully agree with the authors that both funding agencies and researchers are often not critical enough in their assessments of those studies and large grant applications. To date, the studies on neural and psychophysiological correlates not at all contribute significantly, taking into account the large amounts of research funding/resources that have been invested so far. However, why do the authors think that it would be technically, hypothetically, impossible to combine 1PAs with 3 PAs?

Perhaps neural and psychophysiological measurements while the person is aware of and can communicate the mental contents to others (if requested or desired) could still add important clinical information (e.g., neural and psychophysiological measurements while patients with depression fill in the BDI-II)? In line with this, the authors write on page 5 in response to the Urry *et al.* (2004)¹⁰ study “May we use this information to gather more details about what already participants reported in their 1PAs?”, but despite mentioning this question, they further ignore this. In our opinion, they too easily dismiss this option. Therefore, in our opinion, their statement that the neural and psychophysiological correlates “have nothing to add” to the knowledge of these phenomena is too strict and too premature, it might be right, but it could also be totally wrong.

The fourth major point that we would like to tap (see page 6) is the fact that in their discussion the authors focus on the usefulness of biological correlates of 1PAs only. It is true that the biological perspective (significantly marked by the advances in neuroimaging techniques¹¹) is very popular in psychology at the moment; however, we are wondering what the opinion of the authors is with respect to their claims, in terms of the fundamental laws of physics¹²? Note that to date, a unified brain processing theory (unifying physics and neuroscience) does not exist[ref-13]? How do the authors think that a better theory of its underlying fundamental laws of physics could describe and explain 1PAs and 3PAs? This area might build a bridge in the understanding of 1PAs and the underlying mechanisms that are partly measured by 3PAs.

Finally, there are several minor issues that we would like for the authors to address in their final version of the paper. For instance, the authors should add suitable references behind “Beck Depression Inventory” and “The Structured Clinical Interview for DSM-5 (SCID-5)” (see page 2); moreover, the authors should include higher resolution images of Figure 1 and Figure 2 (see page 3). The authors should write out “NDEs” the first time that they use this abbreviation (see page 4). The easiest way seems to include “NDE” immediately after “Near-Death-Experiences” on page 4. In addition, the authors should take a closer look at “Klein (2015)”¹⁴ on page 4 because there are 3 “Klein (2015)” references (Klein, 2015a¹⁴; Klein, 2015b¹⁵; Klein, 2015c[ref16]) but the authors only use “2015a” and “2015b” (see also the reference list on page 8). Furthermore, the authors should include suitable references behind “space-time and matter-energy”, “Heisenberg’s principle of indetermination” (note it should be “Heisenberg’s” instead of “Heisnberg’s”), and “the concept of entanglement” in order to support their statements (see page 4). The authors should correct the following misspellings/errors on page 2: “be” should be added to the sentence “We will not enter here in the debate about how 1 PAs can also be considered 3PAs”, on page 4: “acording” should be replaced by “according” (see the Reasoning subsection), and on page 5: “helped” should be replaced by “help” and “knew” should be replaced by “know” (see the Hallucinations subsection), “be” should be added to the sentence “that can only be measured” (see the Risk perception subsection), and it should be “which” instead of “witch” (see the Discussion section). Also we would suggest adding a “Conclusion section” to the paper at the end of their paper (on page 6) and or alternatively at the end of the Introduction section of their paper. The last minor revision is that the authors should add a “s” behind the word “author” in the Author contributions section of their paper.

To conclude, the present opinion article¹ is definitely worth publishing and will stimulate further discussion on how to best investigate and use research money and resources in the study of 1PAs and 3PAs. Moreover, the future will show whether the authors are correct in their claim that even a complete description of the brain and psychophysiological correlates of these 1PAs does not add

any further information about their contents and characteristics.

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Is the topic of the opinion article discussed accurately in the context of the current literature?

Partly

Are all factual statements correct and adequately supported by citations?

Partly

Are arguments sufficiently supported by evidence from the published literature?

Partly

Are the conclusions drawn balanced and justified on the basis of the presented arguments?

Partly

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 30 Apr 2017

Patrizio Tressoldi, Università di Padova, Padova, Italy

Thank you for your accurate and constructive review and sorry for the multiple typos. In the following we try to answer to all your main comments.

- ...self-rating instruments, such as the Beck Depression Inventory-II (BDI-II)2, have their own limitations... how should psychologists/psychiatrists deal with those methodological limitations in daily clinical practice according to the authors? In our opinion, relying on those (structured) questionnaire outcomes only, does not seem the way to go.

Reply: we acknowledged the limitations of all instruments and procedures for a complete assessment of 1PAs expanding the paragraph "First-person accounts are not always reliable" now moved before the Discussion. However, these limitations cannot be offset by 3PAs, but only improving the instruments and procedures for the knowledge of 1PAs, see for example Pastore M, Nucci M, Bobbio A and Lombardi L (2017). Empirical scenarios of fake data analysis: The Sample Generation by Replacement (SGR) approach. Front. Psychol. 8:482. doi: 10.3389/fpsyg.2017.00482; Lange R. Rasch scaling and cumulative theory-building in consciousness research. Psychology of Consciousness: Theory, Research, and Practice. 2017 Mar;4(1):135.

- .. in the years after the Pariente et al. (2005) publication, the measurement of deqi scores of the participants in acupuncture studies were introduced and are now being collected alongside the 3PAs, consisting of the following Deqi sensations: aching, soreness, numbness, fullness, sharp or dull pain, pressure, heaviness, warmth, coolness, tingling, itching, and any others.

Reply: in the "Pain" paragraph we added the procedure used by Hui et al. (2007) for the assessment of Deqi sensations. Their procedure confirms that these sensations can only be investigated by referring to only 1PAs and not 3PAs

- To date, the studies on neural and psychophysiological correlates not at all contribute significantly, taking into account the large amounts of research funding/resources that have been invested so far. However, why do the authors think that it would be

technically, hypothetically, impossible to combine 1PAs with 3PAs?.

Reply: throughout our paper we presented examples where 1PAs and 3PAs are investigated together. However, our main thesis is that they offer very different information and that 1PAs cannot be obtained from 3PAs and hence are primary and irreducible.

- ... we are wondering what the opinion of the authors is with respect to their claims, in terms of the fundamental laws of physics? Note that to date, a unified brain processing theory (unifying physics and neuroscience) does not exist. How do the authors think that a better theory of its underlying fundamental laws of physics could describe and explain 1PAs and 3PAs?

Reply: We agree completely with the necessity to consider valid alternatives to the mainstream physicalism metaphysics as we pointed out in the Discussion. Such new alternatives must not only unify the fundamental laws of physics, that are not those of classic physics, with neuroscience but also with subjective qualia.

- Finally, there are several minor issues that we would like for the authors to address in their final version of the paper.

Reply: thank you very much for all these issues we fixed in the version 2 of the paper.

Competing Interests: I'm the corresponding author

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