Investigating A Hypothesis on The Mechanism of Long-Term Memory Storage

Seyed Amir Hossein Batouli[1,2]*, Minoo Sisakhti[2,3]

ABSTRACT

Memory is a fundamental cognitive function of the human, and long-term memory (LTM) plays a substantial role in it. Despite all the research, the mechanism of the storage of LTM data in the brain, as well as the brain areas responsible for it, are not clearly identified yet. There is an ancient philosophical idea that the human memory is stored in an extracorporeal space, i.e. the human soul. In this study, using a materialistic approach, we aimed to take one step in investigating the role of human soul in brain functionality by assessing the compliance of this old idea with the available neuroscientific facts. Although with the current knowledge of the human it is not possible to accept nor to deny or examine the existence of soul, we think people in the fields of neuroscience, psychology, or psychiatry should start speaking about "human soul" in their works; belief in soul is nearly as old as the history of human, and one day people should start to scientifically investigate it.

Key Words: long-term memory, human soul

Introduction

Memory, as perhaps the most complex function of the human brain, is comprised of multiple fundamental processes, such as perception, encoding, consolidation, storage, and retrieval (Dosher and Ma, 1998; Parle *et al.*, 2006; Nesca and Koulack, 1994). Tulving (Tulving, 2000) has defined memory as "the neurocognitive capacity to encode, store, and retrieve information". If conceptualized regarding persistence, i.e. the length of time the information remains available to us, sensory (working), short-term and long-term memory (LTM) systems are introduced (Atkinson and Shiffrin, 1968; Wickelgren, 1981). These three systems are also different in their capacity: working memory has a limited capacity of only a few items (Cowan, 2001; Miller, 1956), short-term memory keeps small amounts of information for minutes (Ranganath and Blumenfeld 2005), and memories of many events of the lifetime can be found in LTM (Brady *et al.*, 2008; Voss, 2009).

LTM is fractionable into explicit (or declarative) and implicit (or non-declarative) memory systems (Wickelgren, 1981). Explicit memory includes episodic and semantic memories, referring to our capacity to consciously recollect accurate information from the past incidents and remembering their details, and to our general knowledge of the world and facts, respectively (Kompus *et al.*, 2009). Implicit or procedural memory is a non-conscious recollection of information related to skills and is an unexplainable knowledge of how to do things (Ofen, 2012).

A great number of experiments are performed on human memory; however, LTM and in particular

Corresponding author: Dr. Seyed Amir Hossein Batouli

Address: *[1]Department of Neuroscience and Addiction Studies, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran; *[2]Neuroimaging and Analysis Group, Research Center for Molecular and Cellular Imaging, Tehran University of Medical Sciences, Tehran, Iran; [3]Institute for Cognitive Sciences Studies, Tehran, Iran

Tel: +98-21-43052000 (line 159); **Fax:** +98-21-22262049

e-mail ✉ batouli@sina.tums.ac.ir

the mechanism of information storage in it is still an open question in the field of neuroscience (Dudai and Morris, 2013; Tonegawa *et al.*, 2015; Josselyn, 2010). Questions about the location, duration, and capacity of storage, as well as the types of information that are stored, are very critical to be answered. In this paper, we perform a brief review of the current theories on the mechanism of LTM storage in the brain, and also the credibility of the idea that LTM is stored in a metaphysical configuration (human soul) (R.Forsdyke, 2014; Forsdyke, 2009; DRAAISMA, 2000) will be discussed. For a clearer exploration, all functions relevant to the LTM formation are also elaborated.

LTM Storage, Current View

Brain regions are involved in LTM formation, such as ventrolateral, dorsolateral, and frontopolar prefrontal cortex at the frontal lobe (Braver *et al.*, 2001; Ranganath *et al.*, 2003; McDermott *et al.*, 1999), or medial temporal areas and especially hippocampus at the temporal lobe (Schwartz 2014); however, there is no consensus on the specific brain region (s) responsible for the storage of LTM (Teyler and Rudy, 2007). One current suggestion is that memories are distributed throughout the brain (Santini *et al.*, 2014; Schwartz, 2014), and are based on connections across spatially separate areas of it. To precisely answer the questions about "where", we initially have to identify the "how" of memory storage. If a person learns a new fact, and if the brain is believed to be the place of memory storage, then subsequent brain changes or a similar process should happen to mark this new information (Schacter, 2001), regarded as the "detectability criterion" (Takeuchi *et al.*, 2013). The search for the memory spot in the brain started at the whole brain scale (Lashley, 1950), but then the scale decreased to the hippocampus (Scoville and Milner, 1957), individual cells in hippocampus (O'Keefe and Dostrovsky, 1971), synapses (Bliss and Lømo, 1973; Engert and Bonhoeffer, 1999), single proteins (Pastalkova *et al.*, 2006), and even methyl groups (Day and Sweatt, 2011). Two major streams of suggestions for LTM storage are reviewed in below.

Neurons are building blocks of our brain, and therefore they should be involved in any memory-related brain alterations. Synapses are sites of electrochemical communication between neurons, and it was suggested decades ago by Ramo'n Cajal (Cajal, 1894) and by Eccles (Eccles, 1953) that synaptic connections between neurons

are modifiable by learning, and therefore they may serve as key components of memory storage. The structural changes of the synapses (to strengthen or weaken communication between neurons) relevant to LTM storage, known as synaptic plasticity, is reported in many later studies as well (Hebb, 1949; Bailey and Kandel, 2009; Chklovskii *et al.*, 2004; Watson and Buzsáki, 2015). The mechanisms suggested for synaptic alterations include: 1) changes in the strength of connections between synapses (Mayford *et al.*, 2012; Kroes and Fernández, 2012); 2) remodelling of pre-existing synapses, leading to an increase in the number, size and vesicle complement of the active zones of neurons (Bailey and Chen, 1983; Bailey and Chen, 1988b); 3) growth of pre-existing synapses, leading to increase in the number of synaptic varicosities (boutons) (Bailey and Chen, 1988a; Kim *et al.*, 2003; De Paola *et al.*, 2006; Hübener and Bonhoeffer, 2016); 4) alteration in the number of synapses and formation of new ones (Xu *et al.*, 2009; Yang *et al.*, 2009; Moczulska *et al.*, 2013); 5) changes in microtubule turnover and stability (Uchida *et al.*, 2014), and 6) turning nascent presynaptic varicosities into active transmitter-releasing sites (Kim *et al.*, 2003). A recent study has shown that 4.7 bits of information can be stored at each synapse based on the 26 distinguishable synaptic strengths, which were correlated with spine size, the area of the postsynaptic density and the presynaptic active zone, the number of docked vesicles in the presynaptic terminal, and the number of AMPA receptors (Bartol Jr *et al.*, 2015). These changes happen more significantly in engram cells, in comparison to non-engram cells, as they show higher dendritic spine density and synaptic strength due to learning (Ryan *et al.*, 2015; Tonegawa *et al.*, 2015). Engram is defined as the physical basic unit of memory storage (Schacter, 2001).

The best candidate cellular process explaining synaptic changes and strengthening, underlying learning and memory, is long-term potentiation (LTP) (Martinez and Derrick, 1996), which occurs when there is consistent communication between two connected neurons (Schwartz, 2014). Bliss *et al.*, (Bliss and Lømo, 1973) showed that trains of stimulation to the perforant path increased the efficiency of synaptic transmission in the hippocampus of rabbit, suggesting a similarity between LTP and memory mechanisms. LTP also reduces the amount of neurotransmitters forging to the synapse between the two neurons for message

transmission, illustrating the alteration of neuron firing rate due to its experience (Schwartz, 2014).

In another theory for LTM formation, Crick (Crick, 1984) in 1984 hypothesized that LTM storage in the brain needs modifications to DNA and proteins: existing proteins are modified, signals are sent to the nucleus to express specific genes, and new gene products are transported to the synapse where synthesis of new proteins allows synaptic alterations (Bourne and Harris, 2012; Kandel, 2001). In fact, activity at the synapse informs the nucleus to alter transcription (Bailey *et al.*, 2015). The mechanisms involved in this process include mRNA transcription, protein synthesis, mRNA and protein degradation and trafficking, and epigenetic mechanisms, e.g. histone acetylation, DNA methylation, and miRNA regulation (Saab and Mansuy 2014; Jarome and Helmstetter, 2013; Graff and Tsai, 2013; Giese and Mizuno, 2013). As an example, the appearance of Val66Met SNP (single nucleotide polymorphism) on the BDNF (brain-derived neurotrophic factor) gene at the hippocampus showed associations with the time-of-recall measure (Montag *et al.*, 2014), or it was demonstrated that inhibition of protein synthesis interfered with LTM (DINGMAN and SPORN, 1961). It was also speculated that LTM might reside in brain DNA (Bergin 1998), but this idea is currently at rest (Forsdyke, 2009).

A number of limitations are mentioned for the above two theories: the large number of lifetime memories cannot all be stored in the brain by solely growth of new synaptic connections, unless to refine and use older synaptic connections (Bailey *et al.*, 2015); synapses are composed of proteins, and proteins have finite lifetime and need to be replaced with freshly synthesized copies (Rosenberg *et al.*, 2014); doubt on the ability of synapses to preserve their individual characteristics for extended durations (Rosenberg *et al.*, 2014); different timing and level of response to learning and memory in dendritic spines (Restivo *et al.*, 2009; Lai *et al.*, 2012); synapse to nucleus communication being challenged by the time and space constraints (Rosenberg *et al.*, 2014); a trade-off between memory strength and memory lifetime in the synaptic change model: highly plastic synapses good at storing new memories, but poor at retaining information, and vice versa (Roxin and Fusi, 2013); and the synaptic plasticity model being unsatisfactory regarding kinetics, compactness, lack of information theory, and energy requirements (Gallistel and King, 2009).

Further questions are also raised about the role of synaptic plasticity in the memory consolidation: are structural synaptic changes a consequence of learning, or only a correlation? Are memories stored over time in the same or different synapses? Is LTM stored in the synapse, or in the nuclear programs within the soma? What are the relative contributions of protein redistribution and synthesis to synaptic plasticity? Which proteins, if any, are synthesized for the consolidation process? How long does it take to traffic the proteins to remote synapses, and how are they targeted to specific synapses?

A recent study has shown that our brain can store ten times more information than we thought, in the form of synaptic plasticity (Bartol *et al.*, 2015); however, a major limitation of this theory is reported to be on the capacity of memory storage, i.e. the number of items as well as the amount of information per item that can be stored (Brady *et al.*, 2008). According to an axiom, human's brain is never overloaded for memory storage (Clarke, 2016; Maxcey and Woodman, 2014), but this is difficult to be explained by the current models (Brady *et al.*, 2008). Bergin (Bergin, 1998) declares that brain has around 10^{11} neurons, each with 10^3-10^4 synapses, which makes it unlikely that the synaptic plasticity alone could explain storage of such an enormous amount of lifetime information. Also, if a neuron is going to only store the history of its own action potentials, considering an average lifetime of 10^9 seconds and 10Hz frequency, it should store 10^{10} bits of information, and there are doubts on this ability (Bergin, 1998). In the mid-1950s, von Neumann (von Neumann 1958) calculated that $2.8×10^{20}$ bits of information (around 10^{11} CD-ROM discs) should be stored for an average human lifetime, and therefore he made doubt on the ability of the brain to have such storage capacity. Due to the above limitations, it is inevitable to consider other hypotheses for the mechanism of LTM storage (R.Forsdyke, 2014).

Human Soul

It is argued that physical *vs.* metaphysical explanations of the scientific phenomena should only be alternatively used; as an example, offering explanations for evolution reduced faith in creationism (Shariff *et al.*, 2008; Lawson and Weser, 1990) and weak theories bolstered belief in supra-natural beings (Preston and Epley, 2009). Similarly, Preston (Preston *et al.*, 2013) found that belief in soul decreased when neuroscience provided strong explanations for the mind, and enhanced with gaps

62

in neuroscience. One reason is the supposition that everything should only be empirically substantiated in order to be believed (Turner 2015). Beginning with the Renaissance, as religion did not match with the language of science, i.e. not being measurable or quantifiable, was gradually marginalized and separated from science. It is reported that metaphysics can sometimes provide interesting ideas for the scientific questions, however, they are usually refused to take as serious due to the above separation (Moreira-Almeida, 2016). As a result, a reunion of physics and metaphysics is suggested (Dennett 1991; Nagel, 1974), and as Haught (Haught, 2005) has discussed, many of the great founders of the modern science did not believe that science is not separable from material.

The human soul is defined by Aristotle as the first actuality of a natural body that is potentially alive (Jannone, 2002), or as an immaterial entity that represents an individual's essence (Richert and Harris 2006). It is said to be immortal; unitarian, compact and unilateral; pre-existing birth and surviving death; bearer of knowledge and truth; personal and the source of our volition; more or less bound to bodies, and in constant struggle with the body (Plato); persisting across physical transformations and travelling independently of the body; and being cognitive in its essence (Anon n.d.; Boyer 2001; Karasmanis 2006). According to the dualist philosophical perspective (Plato, in Phaedo), soul and body are separate entities: souls, embedded in bodies, enter into the immaterial world after death. Aristotle claims that souls are made from different substances than bodies, but he added that souls cannot exist independently from the body; Aquinas (Aquinas, 1912) believed that people are whole only when their soul and body are united; and the Persian philosopher, Avicenna, in his "compendium of the soul" defined soul as the speaking or rationa power. Descartes (1641), in his modern dualist perspective, promoted that mental and material substances are separate: mental substances have no extension in space, but materials cannot think, and this dualism is compatible with the existence of immortal souls (Anglin, 2014).

There are arguments provided as proofs for the existence of soul, including the "nonlocal mind" concept, defined as information transfer into/from the mind without mediation by the physical senses (Dossey, 1987); the mind-body (Ward and Wegner 2013; Forstmann et al., 2012; Gray et al., 2011) and

soul-body (Ryle 1949; Burris and Bailey, 2009; MILLAR, 1936) dualisms; the separation of the subjective experience from physical events (Wegner, 2003); the mediumship experience, i.e. having contact with non-material entities (Bourguignon, 1976); and the near-death experience (NDE), in which people have out-of-body perceptions (van Lommel, 2011). A materialistic view seems to be too restricted to explain these phenomena. Ninety percent of the NDE reports were proved to be accurate (Holden et al., 2009); over 90% of adults worldwide believe humans have souls (Bloom, 2007; Uhlmann et al., 2008), and around 24% have felt being in touch with deceased people (Anon, 2006); and many, if not most spiritual traditions in the world believe in soul as a non-material aspect of human being (Hufford, 2010).

Perception

Here, we begin elaborating our model in which the human soul may play a role in LTM formation. Perception is the front line of gaining knowledge from the surrounding environment, through the five senses of sight, hearing, taste, smell and touch (Earl, 2014). The sequence of events in perception includes the collection of information by the sensory organs (e.g. photoreceptors in the retina for visual perception), transmitting the physiological signals (e.g. through visual pathway fiber tracts) to the relevant brain regions (e.g. visual cortex), and reproduction and interpretation of the signals at the brain (Raz and Levin, 2014). Investigations have revealed different brain regions being involved in the interpretation of various sensory information; examples include medial temporal lobe (Lech and Suchan, 2014), perirhinal cortex (Murray and Richmond 2001), superior parietal cortex (Lidzba et al., 2013) and calcarine sulcus (Raz and Levin 2014) for visual perception, and middle temporal gyrus, dorsolateral and ventral prefrontal, and middle cingulate cortices for touch (Malinen et al., 2014).

Although it seems that a human is continuously collecting information from the surrounding world, the process of perception is in fact happening in discrete time periods, being similar to the sequential snapshots of a camera (Marchetti, 2014; Ungerleider and Mishkin, 1982; Nassi and Callaway, 2009); evidence includes the continuous wagon-wheel illusion (VanRullen et al., 2005; Simpson et al., 2005), the association between light detection rate and state of the process (Latour, 1967), perceived causality (Shallice, 1964), and apparent simultaneity

63

(Hirsh and Sherrick Jr., 1961). There is no consensus on the rate of perception in the brain, however, 24 samples per second is the lowest reported rate. These perceived discrete pieces of information shape the memory, but they need to be encoded first.

Encoding

By perception, the brain receives an enormous amount of data at each time interval; but they should be encoded first, i.e. the perceived data should be associated with its other available data modalities. For example, one may see a phone number written in his/her phonebook, but when remembering, recall the sound of reading it. This is because the phone number was originally visually, but at the same time acoustically, stored in his/her memory.

Hippocampus is the main brain region responsible for information encoding (Toepper *et al.*, 2010; Schwartz, 2014; Lech and Suchan, 2014; Kroes and Fernández, 2012). An important characteristic of the hippocampus is its extrinsic connectivity, i.e. being able to integrate information from many distributed neo- and sub-cortical brain regions (Kroes and Fernández, 2012). As formation of memory and especially episodic memory requires integration of information from different modalities which are spread over the cortex (Fuster, 2009; Fries *et al.*, 2003), and as physical connections between distant cortical regions is limited (Markram *et al.*, 1997; Chklovskii *et al.*, 2004) which makes cortical connectivity too sparse to allow associations between all elements of information into one episode (Rolls and Treves, 1998), the hippocampus with its ability to receive data from or project data back to all polymodal areas and many subcortical brain regions (Felleman and Van Essen, 1991) would be an ideal structure for data integration (Rattenborg and Martinez-Gonzalez, 2011). This integration of different modalities of a perceived data into one single episode is regarded as data encoding.

The hippocampus does not receive pure sensory information, but a highly processed multimodal associative information derived from the neocortical areas (Eichenbaum, 2000; Burwell and Amaral, 1998; Suzuki and Amaral, 1994). Indeed, the information passes through the primary and then secondary sensory cortices, association and multimodal association cortices, then the parahippocampal and perirhinal cortices, and at last the entorhinal cortex, before entering the hippocampus (Manns and Eichenbaum, 2007; Simons and Spiers, 2003;

Rattenborg and Martinez-Gonzalez, 2011). The prefrontal cortex, through its connections with the parahippocampal, perirhinal and entorhinal cortices also influences the information in this process (Simons and Spiers, 2003; Eichenbaum, 2000). The output of hippocampus travels via subiculum and fimbria/fornix (Langston *et al.*, 2010).

Data Package

As explained above, associating different modalities of the perceived data together during the encoding phase happens in discrete time periods. Neural computation in discrete times has several advantages, including the temporal precision of information integration and spike-timing dependent plasticity, stabilizing the neural network and its computations, and easier coordination between and within brain regions (Buschman and Miller, 2010). Determining the discrete time periods needs a physiological time measurement phenomena, and brain rhythms are suggested to play the role of a pacemaker in this process (Marchetti, 2014).

Association of different modalities of the perceived data together in discrete times during the encoding phase suggests that the perceived and encoded data are rigorously organized in a structure that we call it a "data package". Consider this as a Microsoft Excel file, in which the rows represent the samples of time, and the columns represent different types of information. As is shown in Fig. 1, in each sample of time, information from all our sensory inputs, as well as internal information such as emotions, are suggested to be recorded in a new row of this data package. Those data that were associated together during the encoding phase are now filled in different columns of one single row of this package, and from this moment, our neural system diagnoses these data in one row to be belonging together. A group of LTM elements which are highly associated together and weakly related to other elements form a chunk (Gobet *et al.*, 2001), and as will be discussed later, the chunking mechanism is highly involved in the retrieval process.

Our suggested "data package" considers that all memories are recorded in an episodic format, i.e. the system is designed to sequentially capture information from all single episodes of our life. Episodic-like storage of memories and attachment of different features of an event to it, such as temporal, spatial, and self-referential features, are suggested in previous studies as well (Winocur *et al.*, 2010;

64

Date	Time	Sample	Spatial	Visual	Auditory	Touch	Taste	Smell	Semantic	Emotion	Attention
…	…	…	…	…	…	…	…	…	…	…	…
…	…	…	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.39	22	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.39	23	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.39	24	Home			Any Data	Any Taste	Any Smell	Any Semantic data	Any Emotion	Level of Tag
2016-05-12	14.12.40	1	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.40	2	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.40	3	…	…	…	…	…	…	…	…	…
2016-05-12	14.12.40	4	…	…	…	…	…	…	…	…	…
…	…	…	…	…	…	…	…	…	…	…	…
…	…	…	…	…	…	…	…	…	…	…	…

Figure 1. The schematic view of the proposed structure for data packages in long term memory storage; each row represents a new and discrete sample of time, and each column represents a different modality of the data that are included in the package. The data that are included in one row of the table are associated together during the encoding process.

Souchay *et al.*, 2013; Brady *et al.*, 2011; Langston *et al.*, 2010). A French psychologist has suggested that memories are gradually reorganized with the passage of time (Ribot, 1977). This "online" information capturing is performed automatically and without human intention (Teyler and Rudy, 2007), which could be an explanation for the ability of humans to clearly remember things that have only once occurred to them (Teyler and Rudy, 2007; Bergin, 1998). Despite that, our suggestion seems to be in contrast with the idea that irrelevant or unimportant data may be prevented from storage (Breton and Robertson, 2014); however, the "automatic recording of experiences" is mentioned as a key characteristic of episodic-like memories (Morris and Frey, 1997), and besides, reorganizing memories in a clear structure is necessary to avoid forgetting (McClelland *et al.*, 1995; Kali and Dayan, 2004).

Hippocampus is responsible for encoding, and therefore we suggest it is also involved in the construction of data packages. Gamma phase synchronization between cortical and hippocampal neurons provides a mechanism in which memory representations from diverse brain regions get encoded into hippocampal representations, and theta oscillations temporally order the representations (Nyhus and Curran, 2010). The role of hippocampus in our suggested mechanism in data encoding and construction of data packages is compatible with many aspects of the "hippocampal memory index" theory (Teyler and DiScenna, 1986), as well as with the "Multiple Trace Theory (MTT)" (Nadel and Moscovitch, 1997; Ryan *et al.*, 2001).

Pineal Gland

Storage of LTM data packages in human soul needs a mechanism for brain-soul interaction, which is the core of the Cartesian dualistic philosophy (Berhouma 2016). One of the first hypotheses on brain-soul interaction has been proposed by Rene Descartes (1596-1650). He raised the issue of soul-body interaction by distinguishing the human to be composed of corporeal and mental substances, the former being subject to the laws of nature, and the latter being totally immaterial (Berhouma, 2016). By this, he established his substance dualism perspective, which explains the existence of immortal souls (Anglin, 2014). He proposed that an organ in the brain, which is pineal gland, is the seat for soul-body interaction; his justifications for that included: this organ not being double in the brain, being placed in the middle of brain concavities which is a very suitable place, being immune from illness, and being highly supported by branches of carotid arteries (Berhouma, 2016). There are other reports about this organ as well: Van Gehuchten called this gland an "enigmatic organ", and believed its role in humans as the connection between the material and spiritual worlds (Pende, 1937); and ancient Indians called it the "third eye", as a window into the spiritual life of individuals (Baker, 1985). The old beliefs and new studies on brain-soul interaction also support the role of an organ such as pineal gland for this interaction: Galen in the 2nd century AD believed that the brain is the center of 'spirit' (Bergin, 1998), and several studies have illustrated that most people believe their self is located at a single point in the body (Alsmith and Longo, 2014; Starmans and Bloom, 2012; Bertossa *et al.*, 2008), more precisely the upper face or upper torso (Alsmith and Longo, 2014), the eyes (Starmans and Bloom, 2012), the brain (Limanowski and Hecht, 2011), or as da Vinci has drawn, behind the eyes in the anterior ventricle of the brain (Perakis, 2013).

65

The pineal gland, suggested as the seat of soul in the brain, is located at the anatomic center of the skull, adjacent to the third ventricle, aqueduct, quadrigeminal bodies and cistern, thalami, velum interpositum, internal cerebral veins, splenium, vein of Galen, and posterior choroidal and posterior cerebral arteries (Sharma *et al.*, 2014). In the 20th C, the link between this gland and psychiatric disorders was more seriously highlighted, with the use of glandular extracts in patients with mental deficiency, as well as with the discovery of melatonin (López-Muñoz *et al.*, 2011).

The sensory information, to be perceived by the brain, should initially be converted to a form identifiable by our neural system, i.e. the so-called electric signals. The same rule applies to the soul. If LTM data packages are to be stored in soul, their conversion to a form compatible with the soul is necessary. This conversion is most suitable to happen at the point of interaction, giving the pineal gland the role of a transducer. However, our brain is limited by its physical nature, and therefore it is only able to produce physical outputs, suggesting that the soul should also have physical properties.

A physical soul is compatible with the immaterial soul hypothesis of Descartes; many other phenomena such as electromagnetic waves or gravitational fields are also considered immaterial in the physical knowledge (Clarke, 2014). There have been attempts to investigate the physical nature of the soul, such as the study which tested body weight before and after death (MacDougall 1907), or the suggestion by C.D.Broad on the influence of mind/soul on brain activity by changing the electrical resistance of the synapses (Broad, 1925), though both these studies suffer from several limitations (Clarke, 2014).

A current more popular explanation for the brain-soul interaction is through quantum physics. The interest towards quantum-based dualism is increased recently to explain paranormal phenomena (Kelly *et al.*, 2006) such as near-death experiences (Carter, 2010; Van Lommel, 2010). Quantum indeterminism has provided a valuable insight into the questions on consciousness (Von Neumann n.d.), as well as free will (Jordan n.d.; Walter, 2001). The clearest and highly cited model for Cartesian dualism based on quantum physics is currently the model of Sir John Eccles, the Nobel prize-winning neurophysiologist (Beck and Eccles, 1992; Eccles, 1992). His model incorporates many aspects of Descartes model and is currently used by the supporters of the Cartesian dualism (Beck, 2008; Hari, 2008; Stapp, 2009), as it postulates self (soul) interacting bidirectionally with the brain (Eccles 1980). As a result, one explanation for the possibility of the soul-brain interaction is through the knowledge on the physical nature of the soul (Clarke, 2014). Identifying details of the mechanism of this interaction needs further studies in the future.

Brain Oscillations

Information transfer requires that the sending and receiving neuronal groups be excited at the same time, and brain oscillations play a significant role in these timings, and especially in LTM formation (Fries, 2005). Oscillations synchronize neurons and enable them to form assemblies, and to effectively send and receive the signals to/from the target neurons (Gray and Singer, 1989; Womelsdorf *et al.*, 2007). There are different temporal scales for the neural interactions; for example, local neural assemblies may communicate with higher frequencies, whereas neurons with long-range connections communicate in lower frequencies (Fries, 2005). A combination of different neural oscillations (frequencies) are involved in performing a cognitive task (Klimesch *et al.*, 2008; Nyhus and Curran, 2010). Brain oscillations are categorized as delta (below 4 Hz), theta (4-7 Hz), alpha (8-12 Hz), beta (12-30 Hz) and gamma (30-100Hz) waves (Niedermeyer 1999).

Brain oscillations play a valuable role in memory (Fingelkurts *et al.*, 2010; Monto, 2012). As for the role of theta rhythm, the behaviour of hippocampus during encoding is organized by theta oscillations driven by generators located in the medial septum and entorhinal cortex interacting with the autonomous theta oscillators of this organ (Buzsáki, 2002; Kocsis, *et al.*, 1999; Goutagny, *et al.*, 2009). The theta rhythm entrains hippocampal cells, and this helps to regulate hippocampal information exchange, as well as the encoding process (Mizuseki *et al.*, 2016; Klausberger *et al.*, 2003; Battaglia *et al.*, 2016). As evidence, the rate of learning in rabbits was observed to be fastest when hippocampal theta power was at its peak (Berry and Thompson, 1978), and in rats, lesions in medial septum disrupted the generation of hippocampal theta rhythm and subsequently the formation of spatial memories (Givens and Olton, 1990; Winson, 1978). The role of theta rhythm in memory encoding, consolidation,

66

and retrieval has also been shown previously (Hyman *et al.*, 2005; Sirota *et al.*, 2003; Isomura *et al.*, 2016; Feeney *et al.*, 2011). Theta rhythm temporally orders the memories, which is essential for the construction of data packages (Buzsáki, 2005; Kesner *et al.*, 2002).

In addition to theta, other brain waves also play role in memory. As the "binding by synchrony" theory proposes (von der Malsburg and Schneider 1986), gamma rhythm firing enables binding of relevant stimulus features together, to provide a coherent pattern of input to the hippocampus. Also, it has been suggested that encoding, temporally ordering of information, and retrieval need an interaction between gamma and theta rhythms (Jensen and Lisman, 2005; Gruber *et al.*, 2008). This interaction, known as theta/gamma code (Jensen and Colgin, 2007), works through a process called cross-frequency coupling (Bragin *et al.*, 1995; Schroeder and Lakatos, 2009), and suggests that neurons do not continuously fire within the theta cycle, but within the theta cycle that is superimposed by the gamma rhythm. Gamma cycles are reported to be more prevalent in short-range neural connections, whereas theta rhythms mostly act in further reaching areas (Gloveli *et al.*, 2005). There are also reports on theta oscillations modulating gamma rhythms in the anterior temporal (Düzel *et al.*, 2003) and hippocampal regions (Mormann *et al.*, 2005). Based on this, it has been suggested that neurons fire only 5-7 times within the theta cycle (Csicsvari *et al.*, 2016; Bragin *et al.*, 1995). Other brain waves, such as delta and beta (Duzel *et al.*, 2005; Mormann *et al.*, 2005), as well as alpha (Klimesch *et al.*, 2004; Mölle *et al.*, 2002), are also involved in the memory process, albeit with less consensus on their role (Osipova *et al.*, 2006; Klimesch *et al.*, 2008).

Sleep and Consolidation

Consolidation refers to stabilization of memory (McGaugh, 2000). During this stage, the labile memory becomes stable and resilient to interferences (Santini *et al.*, 2014). The Standard Consolidation Theory (SCT) proposes that after consolidation, the memory will be represented in a distributed cortical network (Winocur *et al.*, 2010) (represented in the extracorporeal space in the hypothesis here). Consolidation is suggested to happen during sleep (Weber *et al.*, 2014; van der Helm *et al.*, 2011; Ellenbogen *et al.*, 2006; Groch *et al.*, 2013; Ferrara *et al.*, 2006), conceptualized as "active system consolidation" (Vorster and Born, 2015).

During sleep, "replay" of neuronal memory representations occurs in the brain. In rats and rodents, hippocampal cells in sleep showed a pattern of activation similar to the pattern of neuronal activation before sleep (O'Neill *et al.*, 2010; Ji and Wilson, 2007; Wilson and McNaughton 1994). Also in humans, brain activity during the post-learning sleep was determined by the prior task requirements (Gais *et al.*, 2007; Rasch *et al.*, 2007; Sterpenich *et al.*, 2007), and as an example, motor and language learning modulated brain activity in areas related to these functions during the subsequent sleep (Albert *et al.*, 2009; Waites *et al.*, 2005). Replay is observed in many brain regions, including visual cortex (Ji and Wilson, 2007), mPFC (Euston *et al.*, 2007), striatum (Lansink *et al.*, 2009), forebrain regions (Ribeiro *et al.*, 2004), thalamus (Gulati *et al.*, 2014), and the locus coeruleus (Eschenko *et al.*, 2006). It is based on the replay-transfer-potentiation model (Born *et al.*, 2006), which concludes that the consolidated and pre-consolidated memories are identical (Winocur *et al.*, 2010). One explanation for the numerous reports on the connection between the waking experiences and contents of our dreams is the replay of memories during sleep (Wamsley, 2014; Fosse *et al.*, 2003).

Replay of memories is associated with synaptic renormalization. During waking, processing of information occurs in the brain, and due to the synaptic homeostasis hypothesis (Tononi and Cirelli, 2014), the widespread synaptic potentiation occurring during brain operations and especially during encoding alters brain's synaptic weights. The increment of synaptic weight and strength has several costs, including higher energy consumption, increased demand for delivery of cellular supplies to synapses causing cellular stress, changes in support cells such as glia, decrements in selectivity of neuronal responses, and saturation of brain's ability to learn (Tononi and Cirelli, 2014). If these demands were unchecked, the brain would easily reach its operation limits: evidence for this includes the associations of sleep deprivation with poor encoding ability, perceiving reality, and memory, as well as with mood lability, irritability, and psychosis (Yoo *et al.*, 2007; West *et al.*, 1962). Sleep is the time-window which gives the brain the opportunity to carry out housekeeping functions, such as renormalization (downscaling) of synaptic weights (Feld and Diekelmann, 2015; Cirelli and Tononi, 2008), as well as protein translation, refilling presynaptic stores of calcium and glutamate vesicles, resting of

67

mitochondria, membrane recycling, and clearance of extracellular space from neurotoxic waste (Londei *et al.*, 2007; Cirelli *et al.*, 2004; Xie *et al.*, 2013). Therefore, the synaptic potentiation that increases during wakefulness decreases during sleep (Maret *et al.*, 2011).

Synaptic renormalization, in association with the replay of memories, refreshes the physiological capacity of the brain and consequently clears the brain from memory traces. It is suggested in our model that consolidation, happening during sleep, is defined as the operation in which all memory traces are removed from the brain, so that any later retrieval of the memories occur only via one single source: the human soul.

The physiological capacity of the brain is recovered during consolidation, and as a result, numerous reports have shown improvements in cognitive abilities after sleep; examples include the beneficial effects of sleep on information processing and learning (Feld and Diekelmann, 2015), memories with a prospective component (Scullin and McDaniel, 2010), visual texture discrimination task (Karni *et al.*, 1994), intellectual abilities (Gruber *et al.*, 2010), motor and declarative learning tasks (Walker *et al.*, 2002) such as word pair associations and object locations (Wilhelm *et al.*, 2008), gaining insight and finding new solutions to problems (Wagner *et al.*, 2004), encoding performance (Mander *et al.*, 2011), and on many other cognitive abilities (Huber and Born, 2014; Fischer *et al.*, 2002; Rasch *et al.*, 2007).

Consolidation is suggested to happen during sleep; however, sleep has two major phases: slow-wave sleep (SWS) and rapid eye movement (REM). SWS is characterized by large slow waves (0.5-4Hz) and is different from waking rhythms, whereas REM rhythm looks very similar to the waking state and includes gamma waves with smaller amplitude in the neocortex and theta-nested gamma waves in the hippocampus (Watson and Buzsáki, 2015).These phases appear in a cyclical pattern: sleep begins with a light SWS, then a deeper SWS, retreating to light SWS, and concluding with REM, before a new cycle starts (Watson and Buzsáki, 2015). Synaptic renormalization is suggested to happen during REM (Watson and Buzsáki, 2015), and evidence includes correlations between pre-sleep learning, REM sleep duration, and later improved waking performance (Fishbein *et al.*, 1974; Fischer *et al.*, 2002), as well as downscaling of brain's firing rate during the

REM sleep. On the other hand, other brain recovery operations, in addition to the strengthening of critical synapses due to prior learning and brain plasticity, are reported to happen during SWS (Rasch and Born, 2013; Diekelmann and Born, 2010).

Retrieval

Retrieval, in our suggested mechanism, is defined as downloading information from LTM storage on the human soul into the brain level, to remember past events or use the gained knowledge. Retrieval, in general, involves two processes: recollection, an effortful process for searching information by traveling back in time to access that event or knowledge; and familiarity, an automatic process to identify whether an episode had been previously experienced (Donaldson *et al.*, 2001; Tulving, 2002). Retrieval is dependent on having access to cues or traces of the target memories, as using a portion of the memory does activate or replay its entire experience (Teyler and Rudy, 2007).

Retrieval starts by having access to a cue of the target memory; the whole LTM storage will be searched for traces matching with this cue, one or more trace (s) will (may) be identified, the most relevant trace will be selected, and the selected memory will be downloaded to the associated regions of the brain through pineal gland and hippocampus, for further elaborations. However, when downloading a memory, the whole data package relevant to that memory will be downloaded, i.e. those other data that were associated with the target memory during the encoding process. An example would be the situations where smelling a food causes recalling the place it was first tested (de Almeida *et al.*, 2007).

For direct retrieval, the ventromedial prefrontal cortex is the monitoring system responsible for checking task-relevance of the downloaded information in early post-retrieval (Gilboa *et al.*, 2006), and the temporo-parietal junction will signal detection of the task-relevant memory (Ciaramelli *et al.*, 2008). If there is a conflict between the cue and the memory, a more strategic monitoring process, by the dorsolateral prefrontal cortex (DLPFC), may be triggered. After the memory passed this checking, the retrieval attempt stops (Schacter *et al.*, 2007). For indirect retrieval, as the target memory is not elicited by the cue, the ventrolateral prefrontal cortex selects the cues needed to gain access to the memory (Badre and Wagner, 2007), and the DLPFC will manage the memory search. The cycle of cue specification

68

and memory search continues until the retrieved information matches the desired memory. This procedure is mostly in agreement with the "pattern completion" process suggested as a memory recall process (Marr, 1971), and with REMO (retrieval mode), a neurocognitive task set that is necessary for episodic retrieval (Lepage *et al.*, 2000).

The principle for a successful retrieval is cue-trace compatibility, or the encoding-retrieval match, defined as the similarity between retrieval cues and the previously encoded data (Nairne 2002). This match states that the conditions present at retrieval should have overlaps with the conditions that existed during encoding (Tulving, 1983). The increment of this match improves memory performance, as it indicates a higher probability of identifying memory features/traces that predict the particular target (Nairne, 2002). However, although the cue-target match is necessary, it is not sufficient for retrieval; a cue may match with more than one target memory, and therefore it is the "relative" match that is important. In other words, knowing the overall value of the match between a feature and an event is not informative about the material of retention, unless a comparison between the values of other matches happen (Nairne, 2002). This is referred to as "cue overload", defined as how uniquely a cue predicts a target memory (Roediger and Guynn, 1996).

In addition to the data, the brain regions that are involved in encoding and retrieval also match (Weber *et al.*, 2006; Henson and Gagnepain, 2010). It is observed that those sensory brain regions that were active during encoding of perceived information are also active during retrieval of the same information (Wheeler *et al.*, 2000; Prince *et al.*, 2005; Daselaar *et al.*, 2008). Examples include the emotion-, memory-, and sensory-related brain regions that are active during both processes (Addis *et al.*, 2004; Greenberg *et al.*, 2005; Rubin, 2005).

Familiarity check happens during retrieval, and in our hypothesis it is referred to non-intentionally comparing all our perceived data with the contents of the LTM storage, to signal any similarity/differences between them. An example would be the situations that one instantly figures out that something is changed in a place, or a friend sounds sick, with no intention to compare that scene or sound with his/her memory. This is compatible with the conceptual short-term memory theory, declaring that when a stimulus such as a picture, object, or a word is

perceived, it is instantly identified and the relevant information from LTM is activated (Potter, 2012). Recognition (Rahm *et al.*, 2014; Hollingworth, 2003), retrieving the meaning of a word when reading a sentence (Ullman, 2001), or a proper and quick decision making also rely on matching sensory data with the LTM representations. The time order for the availability of information during this process is within 100-300 ms (Neely, 1991; Potter *et al.*, 2010). This is a necessary component of the implicit memories retrieval, such as a procedural memory, in which people perform a task without any conscious endeavour for retrieving the relevant information.

Hippocampus, due to its significant role in retrieval, is called the "central organ to recall" (Squire, 1992). This organ is active while memory retrieval occurs (Brodziak, 2013; Ryan *et al.*, 2001), and it indexes the parts of the brain that should be activated to accommodate the portions of the downloaded data package (Nadel and Moscovitch, 1997). To be more precise, hippocampus receives data from the pineal gland, re-encodes it (Winocur *et al.*, 2010), and spreads the information to the relevant brain areas for further elaborations (Daselaar *et al.*, 2008), or to re-instantiate the initial experience (Rattenborg and Martinez-Gonzalez, 2011).

Despite the reports on a corrupted retrieval due to hippocampal damage, such as in patients G.D., R.B., and L.M. (Rempel-Clower *et al.*, 1996), a resected hippocampus while a successful retrieval is also observed, such as in patient H.M., who had a considerable capacity to remember the memories related to before his hippocampus surgery (Squire, 2009). It seems that due to brain plasticity, other brain areas do help in retrieval when the central responsible organ is damaged. The suggested areas here include amygdala, mammillary bodies, mediodorsal nucleus of the diencephalon (Zola-Morgan *et al.*, 1986), and the entorhinal, perirhinal and parahippocampal cortices (Zola-Morgan *et al.*, 1994). Formation of these parallel paths take time. As is reported about patient R.B., his memory was much better after 23 months of his injury, compared to after 6 months (Zola-Morgan *et al.*, 1986).

Attention

All perceived information are stored in LTM; however, this does not imply that all the information relevant to a cue will be downloaded during retrieval. In fact, only those information that were in the focus of attention are retrievable (Meuwese *et al.*, 2014). This

69

is a mechanism for downloading important data for processing and ignoring irrelevant data, due to brain's limited processing capacity (Luck and Vogel, 1997). In our suggested mechanism, only the "tagged" data packages are retrievable, and we propose the "tags" to be either based on attention or time.

Attention is a mechanism enabling us to cope with the limits of our sensory, perception and processing networks (Marchetti, 2014). Saliency refers to the prominence of an object relative to its background, e.g. the level of difference between the features of a visual target and its surround (Treisman and Gelade, 1980). Salient objects capture the attentional load of our perception system, and few examples of saliency include novelty (Wittmann *et al.*, 2007; Klebaur *et al.*, 2001), emotion (Talarico *et al.*, 2004), repetition (Gonsalves *et al.*, 2016), familiarity (Poppenk *et al.*, 2010), and uniqueness (Hadley and MacKay, 2006).

Attention has a significant role in encoding and retrieval of LTM; evidence includes the items at the center of attention being retrieved more easily and efficiently (Cowan, 2011); items should be in the focus of attention to be remembered (Oberauer, 2002); more easily, more reliable and more long-term remembering of emotionally salient information compared to neutral information (Anderson *et al.*, 2006); increment of salience in an item resulting in poorer memory performance for other less-salient stimuli (Melcher and Piazza, 2011); and better memory for colour, location, or visual details of emotional items, compared to non-arousing items (MacKay and Ahmetzanov, 2005). On the other hand, there are reports on the decline of memory performance with attentional distraction (Dolcos and McCarthy, 2006) such as in in-attentional blindness (Simons and Chabris, 1999), as well as on association of forgetting with insufficient attention at the time of encoding (Simons and Levin, 1997), or in patients with a lesion in the parietal lobe due to disruption of their attention network (Berryhill *et al.*, 2007).

The level of attentional load of each stimulus is also recorded in the LTM data package. A few brain areas determine this burden, by providing attentional biasing of sensory data and emotional features of memories, including the prefrontal cortex (PFC) (Hopfinger *et al.*, 2000), amygdala (Dolcos *et al.*, 2004), superior parietal lobe along the intraparietal sulcus, inferior parietal lobe at the temporo-parietal junction (Ciaramelli *et al.*, 2008), and hypothalamus

(Schwartz, 2014). Among all, as amygdala is highly connected to the hippocampus, its contribution in data package construction is considerable.

The second tagging mechanism is time-tagging, which declares that all perceived data are retrievable in a short period of time after their perception, even if they have no attention-tagging. The data which lack attentional load will not be consciously retrievable after this period. Jeneson and Squire (Jeneson and Squire, 2012) have considered time-tagging as a special kind of attention that diverts through the passage of time. Although based on Ebbinghaus's curve most memories fade in time (Moser *et al.*, 2015), based on our suggested mechanism all memories can be recalled over a short period after their perception (time-tagging), and any later retrieval requires attention tags.

Conclusion

Ervin Laszlo, a contemporary scientist, does have valuable ideas with which our theory agrees. He has important publications on near-death experiences and on the limitations of the turbine theory of consciousness, and he believes that the consciousness is nonlocal (not confined to the brain), is "saved" beyond the living brain, it is the soul or spirit that we communicate with when we encounter an entity that appears as a living consciousness, and the consciousness may be in a realm beyond the spacetime, due the latest theories in quantum physics which suggest there is a deeper dimension in the cosmos. Consciousness could reside in that dimension, and only manifest itself in space and time. In the words of Giordano Bruno, the infinite universe is filled with an unseen substance called aether or spiritus, and Laszlo suggests that all things that emerge and evolve in space and time are holographic projections of a deeper dimension. In sum, he believes that consciousness is not part of the brain and it is not produced by the brain, and is a cosmic phenomenon temporarily associated with a living brain (Laszlo, 1972b; Laszlo, 1972a; Laszlo, 1987; Laszlo and Peake, 2014; Laszlo, 2014).

In this study, we evaluated the hypothesis on the role of human soul in LTM storage. We initially reviewed few current theories on the mechanism of LTM storage, and showed that their limitations have left this mechanism mysterious. Human soul and the evidence on its existence were discussed, and later, to draw a comprehensive picture of the hypothesis, all relevant brain functions which play a role in LTM formation were elaborated.

There are a few issues which should be considered here. I) Several details of the presented hypothesis are not covered here. Our major aim in this paper was only to share the general skeleton of the hypothesis, and elaborations on its further details need subsequent publications. II) Our hypothesis does not ignore the substantial role of the human brain in our daily life and in functions such as information processing, decision making, actions and communications. However, the hypothesis proposes that all these functions are the products of a successful bi-directional interaction between brain and soul. This is similar to a TV which plays movies using the data received through the electromagnetic waves (van Lommel, 2011). In other words, it is suggested that the brain is mostly a processor, not a source of information. III) Neurotheology, the term introduced by James Ashbrook, is a field of science which tries to put theories from neuroscience and theology together, using credible evidence of both sides (Shukla *et al.*, 2013). Merging these two should not be a fear for people of either of the sides (Freris, 2013). Currently, many neuroscientific ideas are considered as a metaphor, and only a fruitful cooperation between these two fields may reveal the truth of the ideas and lift our eyes to new horizons.

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78

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79