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LETTER TO THE EDITOR

Biophotonic Activity and Transmission Mediated by Mutual Actions of Neurotransmitters are Involved in the Origin and Altered States of Consciousness

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Dear Editor

Despite remarkable advances in our understanding of brain functions, the neural substrates and correlates of consciousness remain unclear [1]. It has been argued that classical physics is intrinsically incapable of explaining the holistic aspects of consciousness, especially its hard problem: phenomenal consciousness (P-consciousness) [2]. Several theorists have therefore proposed quantum mind theories of consciousness such as the Orch-OR (Orchestrated objective reduction) theory [3]; they offer descriptions of P-consciousness and interpretations of access consciousness (A-consciousness) based on quantum mechanics or quantum models. Recent experimental findings have suggested that biophotonic activity and transmission in neural circuits may be involved in the higher brain functions associated with consciousness and may play an important role in the generation of the quantum mind [4–6]; however, the underlying mechanisms are far from being understood.

Although there are disagreements regarding the categorization of consciousness, it has been widely accepted that in human beings it can be divided into sub-consciousness, unconsciousness, and consciousness, and animals may also have similar states [7]. Many studies have shown that neurotransmitters and their receptors in the brain have close relationships with altered states of consciousness. Acetylcholine (ACh) plays an important role in the enhancement of alertness, in sustaining attention, and in learning and memory. Dopamine (DA) contributes to the action-selection process and plays roles in the decision-making and reward systems. The effects of norepinephrine (NE) manifest as alertness, arousal, and readiness for action. 5-Hydroxytryptamine (5-HT) regulates mood, appetite, and sleep, as well as some cognitive functions, including learning and memory. In addition, theoretical analyses have proposed that 5-HT plays a possible quantum role in consciousness [8]. Therefore, it is interesting to investigate whether the biophotonic activity and transmission mediated by neurotransmitters are related to the origin of consciousness and its different states.

We have previously demonstrated that a long-lasting application of 50 mmol/L glutamate to a mouse brain slice leads to a gradual and significant increase in biophotonic activity and achieves the maximal effect within ~90 min (initiation period) and then presents a stable state for up to several hours (maintenance period) [4]. Here, we found that the mean intensity of biophotonic activity in the early maintenance period (91–150 min) (Fig. S1A, B) not only showed a relatively stable level for a period of days but

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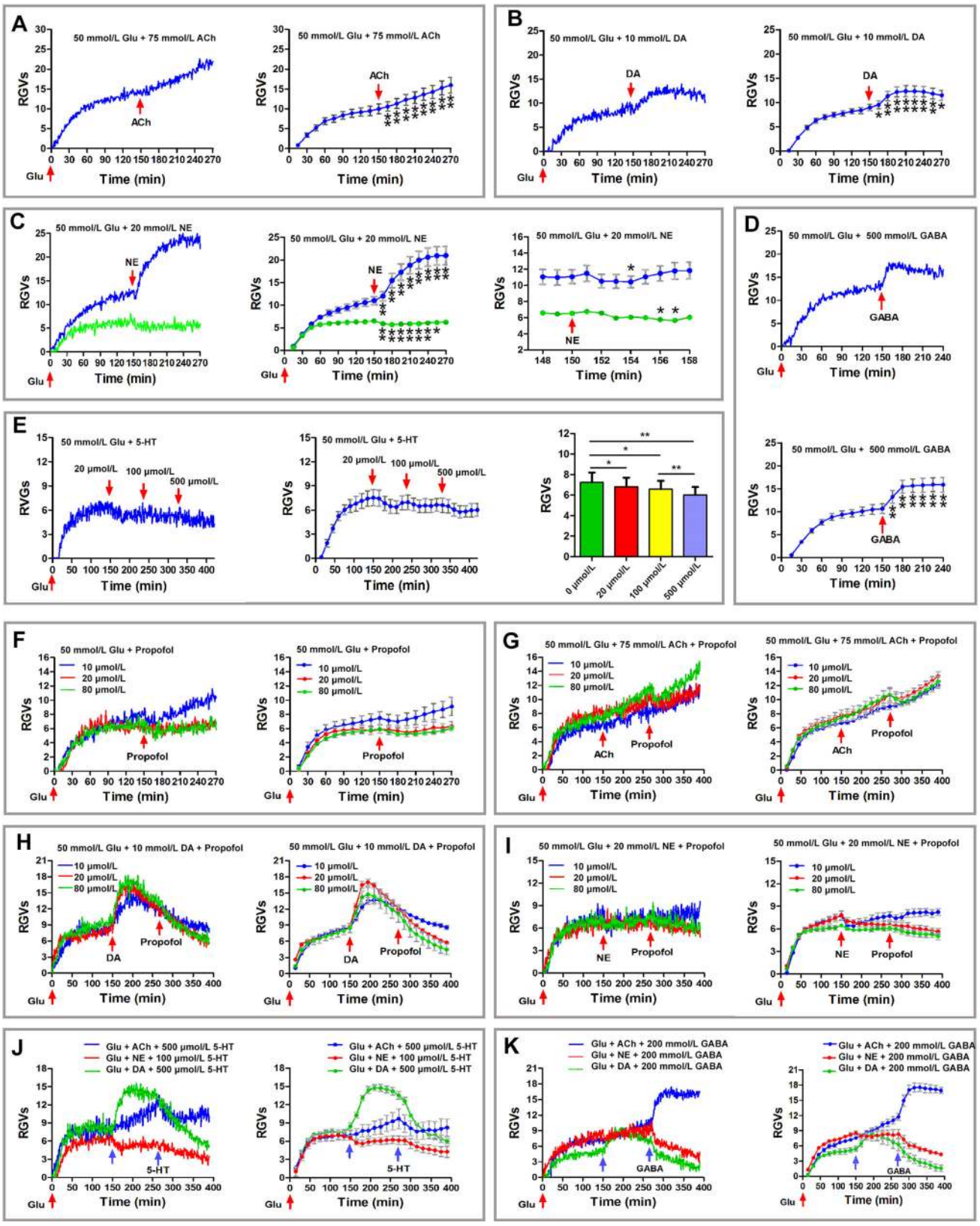
also presented seasonal fluctuations in a one-year-long assessment (from April 1, 2016 to April 2, 2017) (Fig. S1C, Table S2). Therefore, we assumed that glutamate-induced biophotonic activity and transmission may form the basic biophotonic information stream of consciousness and play an important role in maintaining the state of subconsciousness in mice, which appears to show seasonal variation, whereas altered states of consciousness may involve the coordination and regulation of glutamate action by other neurotransmitters.

To test this assumption, we first investigated how glutamate-induced biophotonic activity and transmission are regulated by other neurotransmitters in a standardized mouse brain slice preparation as described in our previous study [4]. A single application of ACh (75 mmol/L), NE (20 mmol/L), or γ-aminobutyric acid (GABA, 500 mmol/L) did not induce glutamate-like biophotonic activity (Fig. S1D, E), although such concentrations of neurotransmitters occur in the synaptic cleft after their release from presynaptic vesicles [4]. We also found that 10 mmol/L DA or 500 μmol/L 5-HT indeed induced glutamate-like biophotonic activity, but the initiation period was shorter and the maximum effects were not sustained for relatively long periods (Fig. S1D, E). However, application of ACh, DA, NE, 5-HT, or GABA to the brain slices during the maintenance period of glutamate-induced biophotonic activity resulted in distinct up- or down-regulation of glutamate action. ACh at 75 mmol/L consistently enhanced the glutamate-induced biophotonic activity (Fig. 1A, Table S3) and DA at 10 mmol/L also significantly enhanced the glutamate-induced biophotonic activity and this tended to decline after reaching the maximum effect (Fig. 1B, Table S3). The synergistic effects of NE at 20 mmol/L depended on the intensity of glutamate-induced biophotonic activity during the early maintenance period (Fig. 1C, Table S3). A sustained enhancement was noticed after a brief inhibitory effect for ∼3 min if the action of glutamate was greater (type I effect) and a slight inhibitory effect was found if the action of glutamate was relatively weaker (type II effect) (Fig. 1C). Interestingly, even 500 mmol/L GABA did not have any inhibitory effect on the glutamate-induced biophotonic activity, but a sustained enhancement of the glutamate-induced biophotonic activity occurred (Fig. 1D, Table S3). Surprisingly, 5-HT at 20, 100, or 500 μmol/L had a sustained inhibitory effect on the glutamate-induced biophotonic activity in a dose-dependent manner (Fig. 1E, Table S3). These findings indicate that, among the classic neurotransmitters, only glutamate can independently induce significant and stable biophotonic activity and transmission, whereas the others (ACh, DA, NE, GABA, and 5-HT) may play a role in enhancing or inhibiting the action of glutamate.

Fig. 1 Individual and synergistic effects of different neurotransmitters and propofol on glutamate-induced biophotonic activity in mouse coronal brain slices. **A–E** Arrows indicate the time points for application of ACh, DA, NE, 5-HT, and GABA during the maintenance period of the action of 50 mmol/L glutamate (150 min). Representative dynamic changes in the biophotonic activity demonstrated by relative gray values (RGVs) in a slice are shown in the left panels in **A**, **B**, **C**, and **E** and in the upper panel in **D**. The sum of the time course of the average change of RGVs from 15 continuously-processed original gray images is shown in the right panels in **A** and **B**, the middle panels in **C** and **E**, and the lower panel in **D**. Application of 75 mmol/L ACh, 10 mmol/L DA, or 500 mmol/L GABA resulted in significant enhancement of biophotonic activity (**A**, **B**, **D**, n = 6 for ACh and DA; n=5 for GABA). Two different effects were found after the application of 20 mmol/L NE (**C**). A sustained enhancement occurred after a brief inhibitory effect for ∼3 min if the action of glutamate was greater (type I, blue line, middle and right panels in **C**, n = 13); a slight sustained inhibitory effect occurred if the action of glutamate was weaker, and a recovery was observed after long-lasting application (type II, green line, middle and right panels in **C**, n = 17). 5-HT (20, 100, and 500 μmol/L, n = 6) significantly decreased biophotonic activity in a dose-dependent manner (**E**, right panel). **F–K** Representative dynamic changes in biophotonic activity measured as RGVs in a slice are shown in each colored line in the left panels. The right panels show the sum of the time course of the average change of RGVs from 15 continuously-processed original gray images. The left arrow indicates the time point for application of glutamate (0 min), ACh, DA, or NE (150 min) (middle), and propofol, 5-HT, or GABA (270 min) (right) in each panel. **F** Glutamate-induced biophotonic activity was slightly influenced by propofol at 10 μmol/L (n = 6) but significantly by 20 μmol/L (n = 10) and 80 μmol/L (n = 6), and recovery occurred after long-lasting application. **G** Sustained enhancement effect of 75 mmol/L ACh on the action of glutamate was not influenced by propofol at 10 μmol/L (n = 4) but significantly by 20 μmol/L (n = 6) and 80 μmol/L (n = 10), and recovery occurred after long-lasting application. **H** The "bell shaped" effect of 10 mmol/L DA on the action of glutamate was not influenced by propofol at 10 μmol/L (n = 6) but significantly by 20 μmol/L (n = 6) and 80 μmol/L (n = 8). **I** The "type II" effect of 20 mmol/L NE on the action of glutamate (see **C**) was not influenced by propofol at 10 μmol/L (n = 6) but significantly by 20 μmol/L (n = 6) and 80 μmol/L (n = 10). **J** The effects of 75 mmol/L ACh, 10 mmol/L DA, or 20 mmol/L NE on the action of glutamate were influenced significantly by 5-HT at 100 μmol/L (NE, n = 4) or 500 μmol/L (ACh and DA, n = 4). **K** The effects of 10 mmol/L DA or 20 mmol/L NE on the action of glutamate were decreased significantly by GABA at 200 mmol/L (n = 4 for DA and NE), and surprisingly, the sustained enhancing effect of 75 mmol/L ACh on the action of glutamate was increased further by GABA at 200 mmol/L (n = 4). Data are shown as the mean± SEM. n = the number of slices from the same number of mice. Two-tailed paired t-tests were used to compare the effects at different time points after treatment and the significant statistical differences (*$P < 0.05$ or **$P < 0.01$) are marked in **A–E**, but not in **F–K**), both of which are explicitly detailed in the Supplementary Material (Tables S3 and S4)

Anesthetics and sedatives selectively erase consciousness or lead to rapid alterations in the state of consciousness from consciousness to unconsciousness or even to coma, depending on the concentration. We chose propofol (2,6-diisopropylphenol), which is a general anesthetic and sedative, to investigate whether it could influence the


A
50 mmol/L Glu + 75 mmol/L ACh
ACh
RGVs
Time (min)
Glu
B
50 mmol/L Glu + 10 mmol/L DA
DA
C
50 mmol/L Glu + 20 mmol/L NE
NE
D
50 mmol/L Glu + 500 mmol/L GABA
GABA
E
50 mmol/L Glu + 5-HT
20 μmol/L
100 μmol/L
500 μmol/L
RVGs
0 μmol/L
20 μmol/L
100 μmol/L
500 μmol/L
F
50 mmol/L Glu + Propofol
10 μmol/L
20 μmol/L
80 μmol/L
Propofol
G
50 mmol/L Glu + 75 mmol/L ACh + Propofol
H
50 mmol/L Glu + 10 mmol/L DA + Propofol
I
50 mmol/L Glu + 20 mmol/L NE + Propofol
J
Glu + ACh + 500 μmol/L 5-HT
Glu + NE + 100 μmol/L 5-HT
Glu + DA + 500 μmol/L 5-HT
5-HT
K
Glu + ACh + 200 mmol/L GABA
Glu + NE + 200 mmol/L GABA
Glu + DA + 200 mmol/L GABA

glutamate-induced biophotonic activity and the synergistic effects of ACh, DA, and NE on the action of glutamate. The low dose of propofol (10 μmol/L), which can induce loss of the eyelash reflex [9], had a transient inhibitory effect on the glutamate-induced biophotonic activity (Fig. 1F, Table S4). A moderate (20 μmol/L) or anesthetic dose (80 μmol/L) of propofol, which has been demonstrated to induce loss of consciousness [9], resulted in a more marked inhibitory effect (Fig. 1F). Although the low dose of propofol (10 μmol/L) did not significantly inhibit the synergistic effects of ACh (75 mmol/L), DA (10 mmol/L), and NE (20 mmol/L) on the action of glutamate, a moderate or anesthetic dose partially or completely eliminated these synergistic effects (Fig. 1G–I, Table S4). The negative regulatory effects of propofol on the synergistic effects of ACh, DA, and NE on the action of glutamate was mimicked by the application of 5-HT at 100 μmol/L or 500 μmol/L (Fig. 1J, Table S4). In addition, the synergistic effects of 10 mmol/L DA or 20 mmol/L NE on the action of glutamate were decreased significantly by GABA at 200 mmol/L, and surprisingly, the sustained enhancement effects of 75 mmol/L ACh on the action of glutamate were increased further by GABA at 200 mmol/L (Fig. 1K, Table S4).

These findings suggest that the classic neurotransmitter systems in the brain play different roles in the origin and emergence of consciousness, considering biophotons as neural signals of the quantum mind. The tonic release of presynaptic glutamate may form the basic biophotonic information stream of consciousness associated with the maintenance of sub-consciousness, and the partial or complete loss of such a subconscious state may result in unconsciousness, coma, or even brain death. Other neurotransmitters, such as ACh, DA, and NE, may contribute to the altered states of consciousness associated with cognitive functions, including learning and memory, language, emotion, the action-selection process, and decision-making, whereas 5-HT might play a role in the negative regulation of conscious states relative to the roles of ACh, DA, and NE (Fig. S2). For example, extensive research has shown that NE-ergic neurons cease activity during rapid eye movement (REM) sleep, which often involves the presence of a dream-like subconscious state [10]. In addition, experimental deprivation of REM sleep in humans and in animals elevates aggressiveness, irritability, confusion, loss of concentration, impairment of memory processing, and memory consolidation, which occur in most neuropsychiatric disorders such as Parkinson's disease, Alzheimer's disease, and schizophrenia. It is surprising that GABA, a well-known major inhibitory neurotransmitter, had enhancing effects on the glutamate-induced biophotonic activity, and even further increased the positive synergistic effects of ACh on the action of glutamate, although significant inhibitory effects on the synergistic effects of DA and NE on the action of glutamate were found. In contrast, the demonstration of 5-HT as a major inhibitor of the synergistic effects of ACh, DA, or NE on the glutamate-induced biophotonic activity may provide a new perspective that would allow a further understanding of the negative regulation of altered states of consciousness and its important role in the pathological mechanisms underlying neuropsychiatric disorders.

In summary, the glutamate-induced tonic biophotonic activity and transmission in different neural circuits in the brain form the basic biophotonic information streams, which represent the quantum state of sub-consciousness or pre-consciousness, called as "Photon quantum mind". The positive and negative regulation of glutamate action by other neurotransmitters may lead to altered states of consciousness, and consequently, quantum computation and information transmission and storage could be realized through biophotonic quantum coherence, entanglement, and superposition based on the interactions of the intrinsic and extrinsic biophotonic information flows. In addition, this study provides new ideas for understanding the pathological mechanisms underlying mental disorders, designing new anesthetics, and developing new drugs for neuropsychiatric disorders.

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Compliance with Ethical Standards

Conflict of interest The authors declare no competing financial interests.

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