

## Anesthesiology's Humanitarian Outreach

*To the Editor:*

Dr. Marchbein's service as president of Doctors Without Borders/Médecins Sans Frontières should make all anesthesiologists proud. The courageous service described in her essay<sup>1</sup> is a stunning example of both the humanitarianism and professionalism of the Doctors Without Borders/Médecins Sans Frontières volunteers. I agree that anesthesiology could contribute more and am happy to report that the American Society of Anesthesiologists (ASA) founded its ASA Charitable Foundation\* in 2011 to support such work. One exemplary group supported by the Charitable Foundation is Lifebox, the foundation implementing the Safe Surgery Saves Lives campaign globally.† Through a combination of introducing oximetry and use of the World Health Organization Safe Surgery Checklist, perioperative complications and hypoxemia can be reduced dramatically.<sup>2</sup> Dr. Marchbein highlights the challenges of technology acquisition in low-resource settings. Lifebox directly addresses this problem by functioning as an intermediary between the oximeter manufacturer and the low-income facilities in need of this technology. The resulting acquisition and delivery cost of an oximeter designed for use in austere environments is \$250. In its first 2 yr of operation, Lifebox distributed more than 6,000 devices under this model and provided training in safe surgery principles to more than 2,000 providers in 90 low- or middle-income countries. The leading anesthesiology organizations around the world, including ASA, are Lifebox partners and demonstrate that the humanitarian contributions of anesthesiologists are tangible and growing rapidly.

### Competing Interests

The author declares no competing interests.

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This letter was sent to the author of the referenced article, who did not provide a reply.

\* Available at: [www.asacharity.org](http://www.asacharity.org). Accessed November 22, 2013.

† Available at: [www.lifebox.org](http://www.lifebox.org). Accessed November 22, 2013.

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## Psychedelics, Glutamate, and Neuroimaging Studies

*To the Editor:*

The article by Icaza and Mashour<sup>1</sup> is a very interesting article because it presents a topic of investigation that is currently attracting the attention of pharmacologists, neuroscientists, and biological psychiatrists around the globe: human research with psychedelic compounds. The text brings important information regarding the history and pharmacology of psychedelics but presents important limitations that are discussed below.

In the first place, by focusing the neurochemistry discussion on *N*-methyl-D-aspartate antagonism and  $\gamma$ -aminobutyric acidergic activity in interneurons, the text narrows its focus and presents limited information regarding the importance of glutamate in the neurochemistry of the effects produced by psychedelic drugs. The head-twitch behavioral response, a mouse behavioral proxy of human psychedelic action, is induced by all psychedelic 5-HT<sub>2A</sub> receptor agonists, and this behavior is decreased in knockout mice for the metabotropic glutamate 2 (mGlu2) receptor.<sup>2,3</sup> Moreover, this receptor has been shown to be expressed in close molecular proximity with the 5-HT<sub>2A</sub> receptor in tissue culture and mouse frontal cortex.<sup>3,4</sup>

Second, Icaza and Mashour<sup>1</sup> affirm that “Only one psychedelic drug—psilocybin—was discussed because this is the only classic psychedelic drug that has been studied with neuroimaging in humans.” This statement is not in line with the literature on psychedelic drugs, which is rich in neuroimaging human studies not only after administration of psilocybin<sup>5</sup> but also after administration of the classic psychedelics mescaline,<sup>6</sup> dimethyltryptamine,<sup>7,8</sup> and the dimethyltryptamine-rich botanical preparation ayahuasca.<sup>9–12</sup>

Finally, the literature on neuroimaging studies and psilocybin is not fully discussed and integrated in the article by Icaza and Mashour. There are important and contrasting data among the studies published to date, and these studies have not been included or discussed. How the decreases in cerebral blood flow and blood oxygen level-dependent signal detected after the intravenous administration of psilocybin in a functional magnetic resonance imaging study<sup>13</sup> can be interpreted in light of the global increases in the cerebral metabolic rate of glucose after oral psilocybin

administration in earlier positron emission tomography studies?<sup>14,15</sup> Is there any pharmacokinetic or pharmacodynamic difference between intravenous and oral psilocybin administration, which could modify the brain's rate of psilocin uptake, changing the neuroimaging patterns observed? These are the types of fundamental questions for future research.

### Competing Interests

The author declares no competing interests.

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### In Reply:

We thank Dr. dos Santos for his interest in our article<sup>1</sup> and his scholarly perspective regarding the neurobiology of the psychedelic state. In response to his comments, our focus on the glutamatergic *N*-methyl-D-aspartate receptor was motivated by the pharmacology of anesthetic drugs that have been more strongly associated with psychedelic experiences in humans; we did not argue that these receptors were the primary molecular targets for psychedelic drugs themselves. In terms of neuroimaging studies, we thank Dr. dos Santos for the additional references and we acknowledge that the article by Carhart-Harris *et al.*<sup>2</sup> is not the only neuroimaging study on the psychedelic state. It would have been more precise for us to state that it is the only neuroimaging study focused on *connectivity* during the psychedelic state in humans. By contrast, the studies referenced by Dr. dos Santos focused on neural activity. The findings by Carhart-Harris *et al.* regarding connectivity allowed us to make comparisons with more recent studies on anesthetic-induced unconsciousness. Finally, we agree with Dr. dos Santos that there are many more exciting questions to be addressed in this area of investigation.

### Competing Interests

The authors declare no competing interests.

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