the realm of respiratory physiology. He instead mounts an ad hominem attack on Davy for his youth and recklessness. If youth truly deserves our censure in connection with scientific discovery, then Haridas must broaden his denouncement. With respect to self-experimentation, undertaken, as Hari-
das observes, at considerable peril, Davy would doubtless hold himself guilty as charged; to Davy, science was exploration, and incidental threats to his personal safety were of little consequence. In this regard, we may perhaps compare Davy’s experiments to those of August Bier and August Hildebrant in spinal anesthesia,2 or of William Halstead in local anes-
thesia.3 Halstead, as a consequence of his studies, struggled with and ultimately overcame cocaine addiction,4 and Hari-
das, in turn, invites us to speculate whether Davy may have been addicted to nitrous oxide. Although Davy’s pattern of
daily nitrous oxide use during his time at the Bristol Pneu-
matic Institute suggests, at a minimum, a maladaptive pat-
tern of behavior, there is no indication either from Davy’s
exhaustive notes, or from the many accounts of friends and
colleagues, that Davy would have met modern criteria for
substance dependence. There is, furthermore, no record of
Davy having consumed nitrous oxide following his tenure in
Bristol. Inexplicably, Haridas equates Davy’s work with ni-
trous oxide to Charles Thomas Jackson’s claims of priority
with ether anesthesia, before abruptly conceding that Jack-
son never published experimental results pertaining to the
anesthetic properties of ether.5

Haridas’ critique ultimately appears to crystallize into one
of pragmatism: Davy, he asserts, was a failure because he did
not put nitrous oxide into practical use as an anesthetic.
Haridas asks us to believe that Davy’s body of work at the
Pneumatic Institute has no intrinsic value: No matter that
Davy conducted and published an unprecedented series of
experiments on nitrous oxide and other inhaled gases, he did not “follow up.” Haridas will have us stop there, but many,
ourselves included, will continue to wonder why not only Davy, but also the innumerable readers of his work, did not
follow up, or why not even Horace Wells’ failed attempt to
demonstrate nitrous oxide anesthesia did not provoke greater
interest in the technique. Science does not exist in a vacuum,
nor do its results always succeed, in the near term, on their
merits; rather it is, and always has been, vulnerable to cultural
credentials and a socially determined sense of possibility. Har-
das chooses to evaluate Davy’s work on strictly utilitarian
grounds and concludes that it was a failure on this basis, in
that it did not lead directly to the development of nitrous
oxide anesthesia. We instead see in Davy’s experiments the
first systematic approach to the evaluation of several gases of
immense practical significance to anesthesiology; it is this
approach which, to our minds, defines the first practice of
anesthesiology as a science, whereby we call Davy the first
anesthesiologist.

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Importance of Body Temperature and
Clinical Data in Behavioral and
Anesthesia Studies

To the Editor:

We have read with great interest the recent article “Anesthetic
Ketamine Impairs Rats’ Recall of Previous Information: The
Nitric Oxide Synthase N-nitro-l-arginine Methylester Antago-
nizes this Ketamine-induced Recognition Memory Deficit,”1
and we would like to address some comments. This study
stresses that nitric oxide metabolism may modify the
anesthetic effects of ketamine. Although this relation has
been described previously, the approach using the
N-nitro-l-arginine methylester (a nonselective nitric ox-
ide synthase inhibitor) to influence the cognitive deficits
induced by the posttraining administration of ketamine
was interesting. Moreover, these effects were observed
only when associated with a change in room temperature,
suggesting that this change is a key factor in this study.

This article referred to the hypothermic properties of ket-
amine; however, hypothermia is usually induced in laboratory
animals by anesthetics in general. Bouladakis and Pitsikas sug-
gested that the effects of ketamine in cognition were dependent
on the room temperature. Importantly, body temperature val-
ues for the tested animals were not shown in this study; instead,
the authors forward the readers to a previous article, in which
initial and 120-min postadministration temperatures in similar
conditions were reported.2 Although we agree that the body
temperature values for animals tested in this study are probably
within the same interval as those reported previously, we
strongly disagree that these measures may be sufficient. Mild
hypothermia values were observed at 120 min after anesthesia in
the ketamine group kept at 21°C when animals were already
recovered. However, it is highly probable that these values may
have been lower during the anesthesia period. Therefore, body
temperature curves throughout time should have been regis-
tered. The report of the body temperature curve would also
dissipate the doubts about a potential hypothermic period in the

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In Reply:

We thank Dr. Valentim et al. for their comments about our article.1 In that work, we did not seek to determine the effects produced by hypothermic ketamine on memory. We sought to investigate the effects of posttraining administration of anesthetic ketamine on rats’ recognition memory and to evaluate whether the nitric oxide synthase inhibitor $\text{N}-\text{nitro-L-arginine methylester}$ (l-$\text{N}$-NAME) was able to reverse the expected behavioral effects produced by anesthetic ketamine. In designing and performing this study, we had two main targets: (1) a clinically relevant anamnetic animal model and (2) producing a behavioral outcome not confounded by other not cognitive parameters (hypothermia, sensory motor factors, etc.). Therefore, anesthetic ketamine’s effects on rats’ memory abilities were evaluated using the novel object recognition task, a behavioral procedure that reflects episodic memory in rodents,2 a type of memory impaired by ketamine in humans.3 Moreover, because ketamine induces hypothermia in rodents, but not in humans,4 it was mandatory for us to assess the effects of anesthetic ketamine on rats’ recognition memory using a condition in which the drug did not display a hypothermic profile. This issue has been investigated in a previous study in which it was revealed that maintaining the animals for 2 h after drug administration at 25°C, but not at 21°C, caused recognition memory deficits without inducing hypothermia.5 Because the condition of 25°C seems to produce results similar to those obtained in humans,3,4 it was chosen for the current experiment.1 Data presented here are in line with studies carried out in humans3 and in rats.5

We do not agree with the authors’ assertion that “this study stresses that nitric oxide metabolism may modify the anesthetic effects of ketamine. Although this relation has been described previously …” Valentim et al., did not provide any source of information about their statement (where has this relation been described?). In contrast to this assertion, the findings reported in our article are innovative because it is the first time to our knowledge that the effects of anesthetic ketamine on posttraining memory components...