animals anesthetized in a room at 25°C. Moreover, it would be helpful to have the body temperature of the animals that received only *N*-nitro-L-arginine methylester, because this substance may have an effect on thermoregulation.[3] Ulugol and colleagues showed that high doses of ketamine and *N*-nitro-L-arginine methylester may cause hypothermia, indicating an involvement of the *N*-methyl-D-aspartate receptor and nitric oxide in the thermoregulation pathway.[3] The authors suggested that ketamine hypothermic properties at a room temperature of 21°C may exert neuroprotection; however, it would be interesting to consider the room temperature increase from 21°C to 25°C as a potential stressful event that increases brain vulnerability and may potentiate ketamine-induced deficit.[4]

It is important to notice that in laboratory animal practice, anesthesia must always be performed under controlled temperature by using a homeothermic blanket connected to a rectal probe. However, the measurement of rectal temperature in awake animals could cause stress and consequently may influence body temperature.[5] To avoid the stress of a rectal probe, the temperature data of an awake rat could be obtained using subcutaneous probes or digital scanners.[6]

Clinical observations, such as respiratory rate, heart rate, and blood pressure, should have been reported because *N*-nitro-L-arginine methylester may induce hypertension; moreover, these hemodynamic parameters may influence the outcome of the study because of potential differences between groups.

Finally, we would like to highlight some differences between humans and animals. This article stresses the hypothermic properties of ketamine and its negative impact on the information previously learned by rats, whereas in humans, ketamine revealed no impairment in retrieval[7] and is known to reduce the possibility of hypothermia.[8]

In summary, our main concerns are related with the lack of data regarding body temperature and clinical information. Possible differences between temperature evolution within groups during the 120-min period may have influenced the results of the study.

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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 *N*-nitro-L-arginine methylester (L-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 amnestic 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 humans[3] 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

(storage and/or retrieval of information) were studied in a recognition memory task in the rat.

Valentim and colleagues correctly claim that rectal temperatures of rats were not recorded in the current work. We did not record animals' body temperatures because our electrical thermometer was out of order. Thus, we referred readers to a previous study of ours[5] (reference 2 of the Letter to Editor by Valentim *et al.* is incorrect) in which the rectal temperatures of animals were registered.

Valentim *et al.* underlined the absence of animals' body temperature curves throughout time in our work. This was not the aim of our study. For us, it was of high priority to establish an environmental condition in which anesthetic ketamine did not induce hypothermia and produced memory impairments in rats. However, we recognize that it would be useful to consider additional experiments that expand our understanding of the role of hypothermia on the effects exerted by anesthetic ketamine on cognition.

Valentim et *al.* pointed out a potential action exerted by L-NAME on thermoregulation. They cited a report[6] in which L-NAME was found to induce hypothermia in mice at 30 and 100 mg/kg, much higher doses than those we used (1–10 mg/kg) in rats in the current article. Moreover, studies carried out in rats have demonstrated that L-NAME has no effect on rats' body temperatures.[7,8] The latter reports[7,8] were unfortunately overlooked by Dr. Valentim and colleagues. This issue has been commented on in the Discussion section of our article.

Concerning the issue that shifting the room temperature from 21°C to 25°C might be a potentially stressful event, this cannot be excluded. This potential stressful effect could occur in all animals independently of treatment if this hypothesis is valid. We previously observed that vehicle-treated animals did not display higher rectal temperatures at 25°C with respect to those expressed by vehicle-treated rats at 21°C.[5] In addition, there is no experimental evidence that ketamine could act in this way.

We agree with the authors' observation that "measurement of rectal temperature in awake animals could cause stress and consequently may influence body temperature". Unfortunately, we did not have available the means (isothermic blankets, subcutaneous probes, or digital parameters) to conduct these measurements. However, we believe that this stress might be common for all rats independently of treatment.

Valentim *et al.* observed that we did not report clinical information concerning the effects of L-NAME on blood pressure. That L-NAME produces hypertension and bradycardia both in humans and rodents is well known. However, we do not intend to report available clinical information about the effects of this nitric oxide synthase inhibitor on blood pressure. The aim of our work was to evaluate whether a potential hypertensive action of L-NAME might have confounded the behavioral outcome of the current study. Thus, the hypertensive properties of L-NAME were taken into consideration in our work and extensively commented on in the Discussion section of our article. The results of our study demonstrated that behavioral consequences caused by a potential L-NAME–induced hypertensive effect likely can be excluded.

A further point is that Valentim *et al.* wonder why we did not include information on the effects of ketamine upon human memory in our article (see the excellent review by Morgan *et al.*).[3] This point is well taken. We did not comment on clinical studies for several reasons. First, those studies do not deal with the amnestic effects of anesthetic ketamine. Second, we preferred to discuss our data with respect to available literature on the role exerted by anesthetic ketamine on rodents' memory.

Finally, the authors correctly report that ketamine does not disrupt retrieval of information in healthy volunteers.[3] The role of ketamine on retrieval abilities of rodents is not yet clarified. In our article, we assessed whether anesthetic ketamine affected the retention trial of the novel object recognition test. Because treatment was applied just after the last sample trial and retention was studied 24 h later, it was impossible to determine on which specific posttraining memory component (storage and/or retrieval) ketamine was acting. Thus, in our work we always strictly referred to "posttraining memory components."

In short, it must be realized that, based on the available clinical information, the purpose of our study was first, to create an adequate amnestic animal model, with good clinical relevance, with the aim of studying the effects of anesthetic ketamine and L-NAME on rats' recognition memory, and second, to obtain a behavioral outcome not confounded by factors other than cognitive ones.

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Is Not High-inspired Oxygen Fraction Really a Risk for Postoperative Pulmonary Complications in Obese Patients?

To the Editor:

In their randomized controlled trial that evaluated the effects of inspiratory oxygen fractions on surgical site infection and postoperative pulmonary complications in obese patients undergoing laparotomy, Staehr *et al.*[1] reported that administration of 80% oxygen compared with 30% oxygen during and for 2 h after surgery did not result in a significant difference in risk of postoperative pulmonary complications. It is generally believed that obese patients have a great respiratory vulnerability because of restricted pulmonary function. Also, respiratory consequences of general anesthesia, surgical incision, postoperative pain, and postoperative medication can add up to this preoperative susceptibility, and render obese patients at great risk of postoperative pulmonary complications.[2,3] In this study, the authors should be applauded for trying to control most of the possible factors that can impact the postoperative pulmonary complications, such as patients' age, smoking history, body mass index, American Society of Anesthesiologists physical status, pulmonary and cardiovascular diseases, methods of anesthesia, type and duration of surgery, and estimated blood loss during surgery. Furthermore, the trial protocol emphasized an optimal perioperative care, especially for epidural analgesia and adequate temperature. However, to differentiate the impact of one factor on the postoperative pulmonary complications in the obese patients, all of the other factors have to be standardized in study design. In our view, three important factors in this study seemed not to be well addressed: proportion of patients with obstructive sleep apnea (OSA), patient's position, and use of chest physiotherapy in the postoperative period.

Obesity is associated with a 12–30-fold increased risk of OSA relative to the normal population.[4] It has been shown that OSA patients are at increased risk of postoperative complications, including adverse respiratory events such as arterial oxygen desaturation and upper airway obstruction.[5] Furthermore, disastrous respiratory outcomes have been reported during the perioperative management of patients with OSA and are a major concern for anesthesia care providers.[6] For this reason, it is recommended to screen patients for OSA syndrome preoperatively, especially for morbidly obese patients.[2]

The article did not specify the patient's position in the postoperative period. Considering the potentially deleterious effects of supine positioning on the pulmonary function in morbidly obese patients, these patients are more optimally managed in a nonsupine position. In this case, there is an unloading of the weight of the intraabdominal contents from the diaphragm, resulting in improvement in pulmonary function and reduction in respiratory complications, including pneumonia and atelectasis.[2] It has been shown that during the first 48 postoperative hours after abdominal surgery, arterial oxygenation of morbidly obese patients is better in the semirecumbent than in the supine positions.[7] Furthermore, morbidly obese patients placed in a reverse Trendelenburg's position have improved pulmonary compliance and increased functional residual capacity, which improves oxygenation relative to the supine position.[8] Thus, we think that in this study, maintained identical positioning in all patients is an important prerequisite to accurately evaluate effect of inspiratory oxygen fraction on the postoperative pulmonary complications.

Similarly, there was no mention of whether chest physiotherapy had been included in the optimal perioperative care of the trial protocol. Chest physiotherapy consists of deep breathing exercises, incentive spirometry, and coughing exercises. In the morbidly obese patients undergoing bariatric surgery, chest physiotherapy has been shown to prevent the reduction of postoperative pulmonary function.[9] Since chest physiotherapy is harmless and affordable, it is recommend to be used as soon as possible during the postoperative period in morbidly obese patients, at least after abdominal or thoracic surgery. Furthermore, chest physiotherapy has been included in algorithm for the postoperative respiratory management of morbidly obese patients.[2]

We believe that if these three factors were also standardized in study design, the results of this study could have been more informative and conclusive.

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