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*Patients expect to receive an anesthetic that prevents the formation of memories during the intraoperative period. Unfortunately, explicit memory formation occurs 40,000 times per year in the United States, while the incidence of implicit memory is thought to be greater. The purpose of the study was to evaluate the effectiveness of word associations as a reliable postoperative indicator of implicit memory formation during the intraoperative period. Forty-eight participants scheduled to undergo general anesthesia for an elective procedure were selected. During the administration of  $0.77 \pm .18 \mu\text{g}/\text{kg}$  per minute of remifentanyl and  $0.31 \pm .04$  end-tidal volume percent of sevoflurane in air/oxygen, word associations in the form of "Trivial Pursuit" (Hasbro, Inc, Pawtucket, RI) game statements were presented via headphones. Within 24 hours of surgery, each participant was given a postoperative word association test that included the experimental and control word associations. No reports of explicit memory were noted. The experimental word associations were correctly answered 19.3% of the time, while the control word associations were correctly answered 12.8% of the time ( $P=.014$ ). The findings illustrated that the word association test in the form of Trivial Pursuit game statements/answers may serve as a reliable postoperative indicator of implicit memory formation during the intraoperative period.*

**Key words:** Anesthesia, implicit memory, Trivial Pursuit, word associations.

# EVALUATION OF WORD ASSOCIATIONS AS A RELIABLE POSTOPERATIVE INDICATOR OF IMPLICIT MEMORY FORMATION DURING THE INTRAOPERATIVE PERIOD

## Introduction

**S**urgical patients who receive a general anesthetic expect that the perception of auditory stimuli will be diminished during the intraoperative period so that explicit or implicit memories will not develop. The expectation usually is met, but in 0.2% or 40,000 of the 20 million anesthetics that are administered in the United States each year, explicit memories of the intraoperative period are formed.<sup>1</sup> Wolters and Phaf<sup>2</sup> define explicit memory as the "conscious recollection of an intraoperative episode as measured by the postoperative interview" and implicit memory as a "consolidated experience that can unconsciously affect one's future performance or behavior." Although the incidence of explicit recall is relatively low, the lingering effects of these memory formations can be detrimental to the patient and healthcare team.

For the patient, psychological traumatic effects of the intraoperative period may lead to a syndrome known as *traumatic neurosis*.<sup>3-5</sup> This syndrome occurs in 10% of all patients who verbalize a conscious awareness of the intraoperative period. These individuals will seek treatment for the fear of dying, nightmares, hallucinations, and the inability to sleep.<sup>6</sup> These clinical symptoms usually are resolved with intensive psychological treatment. The healthcare team faces the risk that the patient may bring forth lawsuits based on the breaching of a contract. In fact, 2% of all malpractice claims are associated with lawsuits stemming from awareness during the intraoperative period. The costs of these lawsuits have ranged from \$1,000 to \$1.7 million, with an average cost of \$195,327.<sup>7</sup>

Similar to the concerns about the formation of explicit memories during the intraoperative period, researchers also are concerned about the formation of implicit memories during the intraoperative period. One reason for this concern is that researchers hypothesize that the incidence of implicit memory formation during the administration of a general anesthetic may be as high as 80%.<sup>8</sup>

In an attempt to quantify the formation of implicit memories, a variety of psychological instruments have been examined.<sup>4</sup> One such psychological instrument being evaluated is the use of word associations in the form of "Trivial Pursuit" (Hasbro, Inc, Pawtucket RI) game statements.<sup>9-11</sup> The use of Trivial Pursuit statements permits the researcher to provide an intriguing auditory stimulus that may be processed into long-term memory and unconsciously retrieved during the postoperative interview. Therefore, the purpose of the present study was to evaluate the effectiveness of word associations, in the form of Trivial Pursuit statements, as a reliable indicator of implicit memory formation during the intraoperative period. Additionally, the findings of the study are clinically important because little research has discussed sevoflurane's effect on the amnesic status of the anesthetized patient.

## Methods

After receiving institutional review board approval, a convenience sample of 48 participants was selected for the study. All participants were scheduled to receive general anesthesia for an elective surgical procedure. If the participant agreed to be in the study, was not on any psychiatric medications, was without a history of intracranial disease or injuries, and had no preexisting

memory deficits, they were enrolled after signing an informed consent. Participants who were scheduled for obstetric, intracranial, or cardiovascular procedures requiring the use of cardiopulmonary bypass were not included in the study.

Each participant was then transported to the operating room and standard monitors were applied. After preoxygenation, induction of the anesthesia was accomplished with 20 mg of lidocaine intravenously (IV), 0.75 to 1.0 µg/kg IV of remifentanyl, 1.5 to 2.5 mg/kg IV of propofol, and 0.4 mg/kg IV of atracurium. A low-pressure, high-volume endotracheal tube was then positioned. The maintenance anesthetic included 100% oxygen, sevoflurane at 0.3 end-tidal volume percent, remifentanyl at 0.6 to 1.0 µg/kg per minute, and an atracurium infusion at 6 to 8 µg/kg per minute. Remifentanyl infusions were adjusted to maintain hemodynamic parameters within 30% of baseline values.

Approximately 30 minutes before emergence from the anesthetized state, 27 experimental Trivial Pursuit statements were verbally presented via headphones to each anesthetized participant during a period of 6 minutes. Each statement was 1 sentence in length, and for every 3 Trivial Pursuit statements, a common word association was expressed. An example of an experimental Trivial Pursuit statement presented to each participant was "Japanese people most strongly associate freedom with the United States." The word association expressed from the use of this root sentence in the 3 different Trivial Pursuit statements was "freedom." The control Trivial Pursuit statements were not presented during the intraoperative period, but tested for during the administration of the postoperative implicit word association test to determine the chance level of providing a correct response. After the statements were presented verbally, the maintenance anesthetic was continued until completion of the surgical procedure. Anesthetic agents were then discontinued, and the patients emerged from anesthesia in a routine manner. All participants were extubated in the operating room suite and then transported to the recovery room.

A research assistant blinded to the study performed the postoperative interview within 24 hours of the participant's arrival in the recovery room. In the initial interview, participants were asked about the formation of explicit memory during the intraoperative period. If the participant had not formed explicit memories, the second phase of the postoperative interview was performed. The second phase involved the administration of the word association test. The word association test consisted of 9 experimental questions and 9 control, or buffer, questions with each question having 5 answers

from which to choose. The research assistant read each question followed by the 5 choices. The participants were asked to select the answer that seemed "most familiar" to them. Responses were then analyzed using the paired *t* test to determine if the word association test in the form of Trivial Pursuit statements could serve as a potential postoperative indicator of implicit memory formation that may have occurred during the intraoperative period.

## Results

Forty-eight participants were selected for the study. All participants received a general anesthetic and progressed through the surgical procedure without incident. Three participants were removed from the statistical analyses because the participants were discharged before completing the postoperative implicit word association test. In addition, 1 participant refused to complete the postoperative word association test. Therefore, 44 participants were included in the data analyses. Descriptive statistics were used in describing the demographic characteristics of the participants included in the study. These findings are noted in Table 1.

Three (6.8%) of the participants had heart disease, 5 (11.3%) had hypertension, 1 (2.3%) participant had diabetes, and another participant had pulmonary disease for which medications were being administered. In addition, the surgical procedures lasted  $89.3 \pm 66.9$  minutes, with 25 (56.8%) patients undergoing abdominal procedures while the other surgical procedures consisted of 3 (6.8%) orthopedic procedures, 5 (11.4%) urological procedures, 1 (2.3%) plastic surgery procedure, and 10 (22.7%) other unspecified surgical procedures.

**Table 1. Demographic characteristics of subjects (N = 44)**

Variable	n	%	Mean ± SD
<b>ASA physical status</b>			
I	11	25	
II	29	66	
III	4	9	
<b>Sex</b>			
Male	13	30	
Female	31	70	
<b>Race</b>			
White	19	43	
Black	25	57	
Age (y)	44		37.9 ± 10.7
Weight (kg)	44		77.9 ± 18.0

Each participant passed the preoperative memory test, received a preoperative medication of 0.2 mg of glycopyrrolate and 1 to 2 mg of hydromorphone intramuscularly, and was taken to the operating room where a general anesthetic was given. The anesthetics agents given during the intraoperative period are described in Table 2.

During the postoperative interview, the 44 participants passed the postoperative attention test<sup>12</sup> without difficulty and denied the development of explicit memories of the intraoperative period. Therefore, the high-dose narcotic, subtherapeutic inhalational anesthetic regimen was effective in providing an unconscious state that was suitable for the implementation of a surgical procedure. In addressing the purpose of the study, the participants provided a correct response rate of 19.3% for the experimental word associations on the postoperative word association test, whereas the control, or buffer, word associations were correctly answered 12.8% of the time ( $P=.014$ ). Thus, the findings illustrated that a surgical patient being administered a high-dose narcotic, with a subtherapeutic inhalational anesthetic regimen, may be anesthetized to prevent conscious or explicit recall of the intraoperative period, but retain the ability to develop implicit memories during the anesthetized state that may be illustrated on an implicit memory test in the postoperative period.

## Discussion

The Trivial Pursuit word association task is a test devised to reveal implicit learning that encompasses the salience of interesting and novel information. The information presented during the anesthetized state is so obscure that the answers are unlikely to be known and must be processed as new information. In using this approach, the results of the present study indicated that the use of the word association test in the form of Trivial Pursuit statements may serve as an

effective postoperative indicator of implicit memory formation that may have occurred during the intraoperative period. The findings of the present study were statistically and clinically significant, although previous studies have demonstrated conflicting results. Reasons for the conflicting findings may be due to the use of an assumption in the present study that may have not been incorporated in the methodological design of previous studies. The assumption was that the neurointegrity of the surgical patient's auditory pathway must remain intact during the anesthetized state for the patient to develop implicit memories of the intraoperative period.

In addressing how this assumption has affected the findings of previous studies, Chortkoff et al<sup>13</sup> administered Trivial Pursuit statements to 22 healthy volunteers in 2 phases with different anesthetic concentrations of desflurane. In the first phase,  $3.9 \pm 0.5$  end-tidal volume percent of desflurane ( $\sim 0.5$  minimum alveolar concentration [MAC]) was given. In the second phase, a targeted concentration of  $5.2 \pm 1.0$  ( $\sim 0.9$  MAC) end-tidal volume percent of desflurane was given to each anesthetized participant. Trivial Pursuit statements were provided to each participant at the different inhalational anesthetic concentrations. One day later, when the postoperative interview was performed, the results indicated no evidence of implicit memory formation at either anesthetic concentration.

One potential rationale for the lack of significant findings was the concentration of inhalational anesthesia administered to the volunteer participants. When the concentration of inhalational anesthesia administered is greater than 0.43 MAC, learning has been shown to be impaired.<sup>14</sup> In addition, Schwender et al<sup>15</sup> found that when the inhalational concentration of sevoflurane increased higher than 0.5 MAC, there were substantial effects upon the neurointegrity of the auditory pathway that may prevent the patient from processing auditory signals into memory that may be demonstrated unconsciously in the postoperative period.

Similar to Chortkoff et al, Gonsowski et al<sup>16</sup> gave desflurane at 0.6 MAC (4.0 end-tidal volume percent) and 1.7 MAC (12.0 end-tidal volume percent) to 12 male volunteers while presenting word associations. The results illustrated that the percentages of correct responses were approximately 20% for the control and experimental groups. Therefore, the present study supports the findings of Gonsowski et al<sup>16</sup> because inhalational anesthetic concentrations higher than 0.5 MAC are assumed to alter the neurophysiological integrity of the auditory pathway and prevent the formation of implicit memories during the intraoperative period.

**Table 2. Intraoperative anesthetic agents administered to subjects (N=44)**

Variable	Mean $\pm$ SD
<b>Induction</b>	
Propofol (mg)	125.7 $\pm$ 35.0
Remifentanyl ( $\mu$ g)	77.7 $\pm$ 12.9
<b>Maintenance</b>	
Remifentanyl ( $\mu$ g/kg per minute)	0.77 $\pm$ .18
Sevoflurane (end-tidal volume %)	0.31 $\pm$ .04
Atracurium (mg)*	75.8 $\pm$ 44.4

\* Atracurium dose includes induction and maintenance.

In contrast to the previous studies, other studies have used anesthetic regimens that preserved the function of the auditory neuro pathways and provided evidence that implicit memories may be formed during the intraoperative period. Adams et al<sup>17</sup> administered a word association test to 25 participants undergoing cardiac surgery. The participants received 44.7 ± 15.0 µg/kg of fentanyl, 0.15 ± 0.06 mg/kg of midazolam, and 0.29 ± 0.16 end-tidal volume percent of isoflurane during the cardiac procedure. During the cardiac procedure, a group of 15 word associations was presented. With this anesthetic regimen, the auditory neuro pathways were not substantially affected, and the participants demonstrated clear evidence ( $P < .001$ ) that implicit memories of the word associations were being formed during the cardiac procedure. Similar findings demonstrating the formation of implicit memories during the intraoperative period, while maintaining the neuro integrity of the auditory neuro pathways, also have been reported by Schwender et al<sup>18</sup> and van der Laan et al.<sup>19</sup>

Thus, the current findings demonstrated that the word association test may serve as a postoperative indicator of implicit memory formation during the anesthetized state, but there is a real urgency to reveal the other factors, such as anesthetic concentrations, specific anesthetic regimens, and/or particular patient characteristics that may explain the phenomenon of intraoperative implicit memory formation. Also, one may ponder how anesthesia providers should currently describe the amnesic status of an anesthetized patient. Should anesthesia providers redefine the amnesic status during an anesthetized state as an unconscious state with the formation of implicit memories that may affect one's performance in the postoperative period or continue to imply to the surgical patient that amnesic status during the intraoperative period is without any form of memory consolidation? Until additional studies provide direction in examining these factors that may lead to the emergence of a clinical instrument that may predict the formation of implicit memories during the intraoperative period, the use of word associations in the form of Trivial Pursuit statements may serve as a postoperative indicator of implicit memory formation during the intraoperative period.

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