Subconscious Auditory Processing in Anesthesia: the Common Theme between Dreams, Implicit Memory and Anesthesia Awareness

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ABSTRACT

The fact that auditory evoked potentials (AEPs) have been used widely as a measure of the depth of anesthesia highlights the importance of auditory modality in consciousness-related neural processing during anesthesia, a phenomena more specifically known as Intra-operative awareness (IOA). The phenomena of IOA has seldom been observed from the perspective of consciousness itself. This perspective is especially important because the dimensions of IOA exist in the subconscious domain of mind as much as they exist in the conscious domain of explicit recall. Two important aspects of these subconscious manifestations of IOA are the implicit recall phenomena and post-operative dreams related to anesthesia experiences. Here we present an integrated auditory-consciousness based model of IOA. We start with a brief description of auditory awareness and the factors affecting it. Further, we proceed to the evaluation of conscious and sub-conscious information processing by auditory modality and their interactions during and after intraoperative period. Further, we show that both conscious and subconscious auditory processing affect the IOA experience and both have serious psychological implications on the patient subsequently. These effects could be prevented by using auditory evoked potential during monitoring of anesthesia, especially the Mid-latency Auditory Evoked Potentials (MLAERs). To conclude, we propose that the use of Auditory evoked potential should be universal with general anesthesia use in order to prevent the occurrences of distressing outcomes resulting from both conscious and subconscious auditory processing during anesthesia.

Key Words: subconsciousness, anesthesia, auditory processing, altered state of consciousness, intra-operative awareness, mid-latency auditory evoked potentials

DOI Number: 10.14704/nq.2014.12.4.752 **NeuroQuantology 2014; 4: 398-405**

Introduction

Importance of Auditory Modality in General Anesthesia

Immeasurable auditory information is continuously processed when we are awake. However, we seldom try to acknowledge the importance of this auditory information processing separately because our awareness is intricately interwoven with our auditory information processing and this tends to keep us in a continuous flow of thoughts. However, when it comes to subconscious/unconscious states like sleep and anesthesia, we are compelled to acknowledge the importance of neural processing and memory of individual sensory modalities. More specifically in anesthetic states, auditory modality seems to be the most important one. The essentiality of auditory processing and memory in anesthetic states is highlighted from the fact that the most common manifestation reported during intra-operative awareness has been vague auditory recall or dreams, both of which result from

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 10 May 2014; **Accepted:** 2 July 2014
***e*ISSN** 1303-5150

auditory processing during anesthesia (Myles *et al.,* 2004). Studies have revealed that as many as 65% of patients report having auditory recalls of intra-operative events during anesthesia (Ghoneim *et al.,* 2009; Schwender *et al.,* 1998). This includes both the explicit and implicit recall of intra-operative events as well as dream-like states. In addition to this obvious importance, auditory processing is known to be both being influenced by and to influence back emotions (Yuri *et al.,* 2007; Fengqiong *et al.,* 2009). Thus it is obvious that auditory perception during anesthesia, both conscious and unconscious would have significant effects on the resultant emotional experiences arising from the events during anesthesia awareness.

In spite of this immense impact that auditory perception has during anesthetic states, it has seldom been highlighted adequately in the literature. Especially, there are no models/theories till this date that aim at integrating all the mechanisms in which auditory perception during anesthesia could lead to/influence anesthesia awareness and its subsequent consequences. Such a model is not only needed for understanding AA, but also for developing better parameters of monitoring auditory consciousness during anesthetic procedures. Our present model here uses a basic consciousness-based approach to understand awareness in anesthesia. Here we incorporate both the unconscious and conscious auditory events during anesthesia as important etiological agents for both the experiences during anesthesia awareness and for the genesis of its subsequent psychological consequences. While taking this approach, we will specifically zero-down to the auditory modality. Our h hypothesis in present article is that auditory processing in both its explicit and implicit forms are the most important individual-related factors contributing to AA and possibly to its late consequences. The clinical implication of our hypothesis is that auditory awareness being the most important variable we need to monitor it for avoiding the occurrence of AA and for preventing its immediate and long-term consequences. For this purpose, we proceed to the last section showing that Mid-latency auditory evoked potentials (MLAEP) are important monitoring tools for assessing the anesthesia awareness as it gives an indication of both conscious and unconscious auditory processing during anesthesia.

Auditory Processing During Anesthesia: A Not So Sleeping Brain

The hallmark of anesthetic state is a significant loss of consciousness/awareness. This leads to an important question: What happens to the subconscious sensory processes during anesthesia? Is there a cessation of subconscious activities during anesthesia as well? Obviously, this is a tough question to answer as the person is not awake to know or reply about his thoughts or emotions. However, a closer look reveals that actually several subconscious processes are very actively working in anesthesia. For example, in the study by (Plourde *et al.,* 2006), the results indicated that one prominent characteristic of loss of consciousness induced by propofol is that specialized, higher order processing areas that normally respond differentially to certain classes of stimuli no longer do so. However, a generalized but attenuated response in primary and adjacent regions persists, as well as a paradoxical response to scrambled words. They concluded that although the highly differentiated neural processes whose outcome leads to conscious perception are either deprived of their normal input or are unable to perform their normal computations thus not all cortical responses are abolished in the unconscious state. It thus seems that the primary and association auditory cortices remain responsive to complex auditory stimuli in a nonspecific way whereas higher-order analytical abilities are paralyzed. These non-specific neural activities can be seen in the context of various subconscious phenomena. Here we highlight two of these important phenomena: 1) Dream related auditory processing during anesthesia and 2) Implicit memory in anesthesia.

Dream-Related Auditory Processing During Anesthesia

Subconscious memories in the form of vague dreams are very prevalent in GA patients. In addition to being prevalent, they are also highly distressing. They may be in fact most distressing events during GA (Utting, 1987; Sandhu & Dash, 2009). In the case series study of 500 patients by Utting *et al.* (1987), 7% of patients considered these dreams to be the worst aspects of their experience as compared to 2% patient who rated the recall of intra-operative (IO) events as the most distressing event. In addition to the fact that dreams are in them distressing, they also increase the chances of actual intra-operative awareness. In a recent study, it was found that IO awareness was 19 times more common among patients who had a dream in comparison to those who did not have those (Samuelsson *et al.,* 2008). In fact, some have conceptualized dreaming during anesthesia as a lighter form of awareness i.e., awareness without explicit recall (Leslie *et al.,* 2007).

Occurrence of these dreams is the most important indicator of the subconscious auditory processing during the anesthesia. But how could the subconscious auditory processing during anesthesia then is conceptualized? For the answer, we turn towards a similar state of consciousness: sleep. From the outset, sleep and anesthesia seem to be very similar. Interestingly, sleep and Anesthetic states of un-awareness also share many common behavioral and neuro-physiological features. Studies of deep sleep using imaging techniques have shown that polymodal association areas are affected more profoundly than unimodal brain areas (Franks, 2008). This functional dissociation implies that during deep sleep the brain can respond to external stimuli via the unimodal areas, but cannot make much sense out of the stimuli due to the inhibition of the higher level processing in polymodal areas. Moreover, some of the polymodal areas which are affected during deep sleep are also deactivated during sedation. This indicates that the final state of anesthesia induced unconsciousness and deep sleep are remarkably similar. This view is further supported by detailed electroencephalographic (EEG) studies that demonstrate similar activity patterns during non-REM sleep and anesthesia (John & Prichep, 2005). These similarities indicate common neural pathways for controlling the arousal of the cortex in conditions of sleep and anesthesia (Lydic & Baghdoyan, 2005). Recent work suggests several candidates for these common arousal pathways. For instance, in both sleep and anesthesia the thalamus may serve as a consciousness switch (Alkyre & Miller, 2005) that disrupts the information flow through the thalamic gateway and triggers the transition between sleep stages. Moreover, sleep and anesthesia are not only supposed to affect the same pathways during unconsciousness but act similarly on these pathways. For instance, the spread of cortical activity is reduced during deep sleep and sedation reflecting a breakdown of cortical connectivity and information flow (Alkire *et al.,* 2008).

In the study by Koelsch *et al.* (2006), under deep propofol-induced sedation, i.e., when participants were unresponsive to normal verbal commands, a tiny MMN was observed in response to frequency and timbre deviants. The MMN was clearly reduced compared to the awake state. The presence of this MMN residual during deep sedation replicates findings from previous studies (Heinke *et al.,* 2004b; Yapparilla *et al.,* 2002), indicating that auditory sensory memory operations are markedly affected by sedation, but can still be observed under deep sedation, even when participants were unresponsive to normal verbal commands. Simpson *et al.* (2002) reported that a frequency-MMN was visible in ERPs recorded during deep sedation, but statistically not significant. The missing significance in that study was presumably due to an insufficient number of trials, which did not produce a signal-to-noise ratio high enough to yield statistical significance (note that in the study the duration of the deep sedation phase was 90 min, resulting in the presentation of 300 deviants per subject in the MMN blocks). Together, the combined evidence suggests that the neural processes underlying the operation of the auditory sensory memory (as indexed by the MMN), and underlying attention-related processes (as indexed by the P3a and the late negativity) are still active, although strongly reduced, under deep sedation (even in subjects that are unresponsive corresponding to MOAAS) (Aceto *et al.,* 2003; Kraus *et al.,* 1995). By contrast, the neural operations underlying the processing of complex, regularity-based structural information (as indexed by the ERAN) are abolished. It is possible that these differential effects of propofol on different cognitive processes are due to differential effects of sedative drugs on separate cerebral structures (Heinke & Koelsch, 2005; Heinke *et al.,* 2004b; Reinsel *et al.,* 2000).

Implicit Memory in Anesthesia

Auditory processing during anesthesia is a very complex process. On one hand, the auditory stimuli perceived during anesthesia may be available for an explicit recall afterwards. On the other hand, the auditory perception may be incorporated into more complicated subconscious awareness like dreams and may be recalled subsequently. The dream-like auditory processing during anesthesia has been described in details in the previous section. Another form of subconscious processing is the implicit encoding of the stimulus. In the study by Aceto *et al.* (2003), an audiotape with one of the four stories was played immediately after intraoperative MLAER recording in patients undergoing laparoscopic cholecystectomy. Explicit and implicit memories were assessed 24h after awakening. Although no patients had explicit recall after the anesthesia, some patients had clear-evidences of priming based implicit recall of the stories told during the anesthetic treatment. Additionally, these patients also had significant AEP correlations which have been described in more details below. These results indicate that not only is the auditory information processed in the form of implicit memory of dreams or dream-like states, but this information also be retrieved by implicit key-word methods.

Subconscious Auditory Processing and Anesthesia Awareness: Three Important Dimensions

In the previous section, we saw that the anesthetic brain still actively processes subconscious information. Now we come to our basic model of the effect of sub-conscious auditory processing on the state of anesthetic awareness. We will explore this association along three dimensions:

1) The effect of emotions on the subconscious auditory processing. To understand this dimension, we will explore the most common physiological state of unconsciousness known: Sleep. We propose that people who are more anxiety-prone have a higher tendency to develop AA because of the fact that they are more prone to wake up to such stimuli which are considered threatening for them, similar to the sleep state.
2) The implicit memory recall. This aspect is particularly important because of the fact that even if the patient is not able to recapitulate the memory explicitly, he tends to carry those auditory impulses in an implicit form, which could be responsible for the long-term psychological consequences of AA.
3) The impact of subconscious auditory processing on other modalities, especially on visual perception. This could have resulted in the visual memories of some cases whose actual perception could have been in the auditory domain during AA.

Sleep: Highlighting the Impact of Emotions on Subconscious Auditory Processing

Sleep is the most common subconscious-unconscious state which we come across at regular intervals as a part of our physiological cycle. Interestingly, sleep and anesthesia share some common characteristics which have been mentioned in more details in the previous section. In this section, we will focus the impact of emotions on the subconscious state of sleep. A very well-known fact is that people become more easily aroused upon hearing their names softly whispered, and a young mother may awaken at the slightest sound emanating from her new born baby. Stimuli implying a potential danger, such as the slight noise of a burglar or of a fire at home, can awaken us, even though its intensity is low. That both the physical qualities of sounds and, even more importantly, the psychological value that people assign to these sounds play a role in awakening is known from studies involving people who live close to airports. Many people regard airplane noise during the night as annoying, implying that they give a high negative value to these kinds of stimuli. The emotional coloring of these stimuli heavily modulates the awakening threshold and arouses people even at very low sound intensities. The sleeping brain is able to automatically detect these kinds of stimuli with a high impact, and these emotional stimuli may trigger a wake-up call (Griefahn *et al.*, 2004; Muzet, 2007).

The discriminative properties of a sleeping brain have been frequently studied by measuring the electrical activity of the brain recorded in evoked potentials. This is commonly done for stimuli not awakening the subjects. Nordby *et al.* (1996), using an oddball paradigm with two tones differing in pitch and probability, found that the representation of auditory stimuli occurred in sleep just as in wakefulness. The prolonged latencies of the components of the event related potentials, however, indicate that the processing of external sensory stimuli is delayed. Karakas *et al*. (2007) also found that the processing of auditory information is slower and takes longer in sleep. Auditory evoked potentials were recorded to frequent and deviant tones by Bastuji *et al*. (1995). During sleep, evoked potentials on frequent and deviant tones closely resembled K-complexes, but the responses to deviant tones were significantly larger than those to frequent tones. *They concluded that the brain is able to detect stimulus deviances during sleep, but also that this detection is less efficient compared to the waking state*. Perrin, *et al*. (1999) presented the subject's own name together with other names to sleeping persons while recording auditory evoked potentials. Indeed, some late components in the evoked responses were selectively enhanced after the subject's own name. *Their interpretation was that the sleeping brain was able to detect and categorize particular aspects of stimulus significance*. The conclusion that the sleeping brain can detect meaningful events in auditory stimuli was highlighted by Portas *et al*. (2000). They showed by simultaneously recording EEG and fMRI in humans, that parts of the prefrontal cortex are more activated by stimuli having a special significance than by neutral stimuli.

This emotional significance of stimulus on subconscious auditory processing could also be responsible for a considerable group of patients suffering from AA. In the study by Ranta *et al*. (1998), three of the five patients with awareness had a history of major depression and also had preoperative symptoms of depression and anxiety. On the other hand, none of the control group patients had any preoperative psychiatric disorders. Such patients could thus be more prone to getting awake from the stimuli of operation theatre due to their underlying emotional tone. Additionally, the stimuli arising in the operation theatre could be easily interpreted as threatening. Both of these factors could be the additional reasons for the frequent awakening especially in patients being administered lighter anesthesia. In addition to higher propensity of such anxious patients of awakening to auditory stimulus, anxiety has also been found to act as a predictor of post-traumatic stress disorder in patients experiencing anesthesia awareness. In the study by Osterman *et al*. (2001), patients experiencing peri-operative dissociative experiences during or immediately after the anesthetic awareness experiences were more predictable for developing PTSD. Dissociation is the result of an extreme anxiety where one feels like moving away from himself or reality in a strict physical terminology. Thus emotions play a very vital role in not only experiencing anesthetic awareness but also for experiencing psychological consequences subsequently.

Implicit Memory in Absence of Explicit Recall

Amnesic patients often exhibit spared priming effects on implicit memory tests despite poor explicit memory. The experiments by Schacter & Church (1995) provide further evidence of spared auditory priming in amnesia, which demonstrate that normal priming effects are not artifacts of low levels of baseline performance, and provide evidence suggesting that amnesic patients can exhibit voice-specific priming when experimental conditions do not require them to interactively bind together word and voice information. This finding indicates that even in patients without explicit recall, the implicit priming during the anesthetic procedure can be carried on which could further add up to the development of late psychological consequences when similar stimuli are presented to the patient. The same can happen if there is some cue-related to the experimental procedure. This may manifest in subconscious way in dreams or as an unidentified negative-emotional state.

The Possibility of Cross-Modal Priming in Anesthesia Awareness

The unconscious auditory processing can have significant effects not only on auditory modality but also cross-modally, for example on visual processing. In a recent study by Lamy *et al*. (2008), they examined whether information perceived without awareness in one modality can bias the processing of information presented in another modality. They used the process-dissociation procedure to distinguish between effects of conscious and unconscious perception, and compared unconscious priming within modality (vision to vision) as well as across modalities (audition to vision). The results revealed significant unconscious priming effects both within and between modalities, with no significant differences between the two effects. In more specific terms, Unconscious cross-modal priming consisting of auditory prime and visual fragment was significant and of a magnitude similar to that of unconscious within-modality priming consisting of visual prime and visual fragment. Thus, information perceived without conscious awareness can nonetheless affect the subsequent information processing of not only the same but also in a a different modality. From a psycholinguistic viewpoint, the finding that a spoken word perceived without awareness can prime that word in visual form is open to different interpretations. Heard words may be connected to seen words through direct phonology-to-orthography links or via the mediation of semantic representations. The presence of cross-modal priming suggests that activation of at least one of these two levels can occur without the requirement of a conscious control.

This kind of cross-modal integration of subconscious processing could result in at-least some cases of the visual recall of the operation-related stimuli which could actually have been processed through auditory stimulus during the operative procedure.

MLAEP and Auditory Consciousness during Anesthesia

The Auditory evoked potential (AEP) is categorized on the basis of the latency of the response following the auditory stimulus. For example, the auditory brainstem response (ABR) occurs in the first 20 ms after the stimulus, the middle latency response (MLR) from 20 to 70 ms, and the slow vertex response (SVR) up to 500 ms after stimulation. The midlatency auditory evoked potential (MLAEP) is generated as the auditory signals pass through the primary auditory cortex, perhaps with some additional contribution from the mesencephalic structures such as the medial geniculate (Jacobson *et al.,* 1997; Deiber *et al.,* 1988). In the review by Pockett (1999), the empirical work was reviewed which correlated the presence or absence of various parts of the auditory evoked potential with the disappearance and reemergence of auditory sensation during induction of and recovery from anesthesia. From her review, she put forth the hypothesis that the electrophysiological correlate of auditory sensation is whatever neural activity generates the middle latency waves of the auditory evoked potential. Review related evidence suggested that earlier or later waves in the auditory evoked potential do not co-vary with auditory sensation (as opposed to auditory perception) and it was therefore suggested that they are possibly not the electrophysiological correlates of auditory sensation.

Midlatency auditory evoked response (MLAERs) monitoring has been proposed as a measure for ascertaining the adequacy of the hypnotic state during surgery (Drummond 2000; Loveman *et al.,* 2001). This adequacy of hypnotic state has been conceptualized as a complete awake state with response to verbal commands. Because the primary auditory cortex processes incoming acoustic signals as simple sounds (Zatorre *et al.,* 1992) it is thus not surprising from the audiological standpoint that the patients with attenuated MLAEPs have been found to be unresponsive to verbal commands. However, MLAERs are also effective in assessing subconscious auditory processing. This processing involves sound registration and a complex mechanism of implicit memory processing (Kraus & Me Gee, 1995; Merikle & Daneman, 1996). This close relation between the MLAEP and the responsiveness to verbal command indicates that there is tight correlation between the functional integrity of the MLAEP neural generators and the responsiveness to verbal command during anesthesia. The MLR has been suggested as a possible indicator of depth of anesthesia, although it is not known whether the click stimulus itself affects the level of arousal of the patient. Several studies have reported changes in the response with anesthesia. The study results by Schwender and colleagues whose patients with implicit memory for a tape of the story of *"Robinson Crusoe"* played during anesthesia showed preservation of the MLAERs, while in patients without implicit memory the MLAERs were severely attenuated, indicating that auditory stimulus processing was blocked at the level of the primary auditory cortex. Of Schwender's patients who showed priming, all exhibited a Pa latency increase less than 12 ms during anesthesia (Sender *et al.,* 1994). Similarly, in the study by Aceto *et al.* (2003) it was found that during deep general anesthesia in patients without subconscious awareness, the MLAERs were suppressed or attenuated. In contrast, in patients with subconscious awareness, MLAERs showed a wave pattern similar to the awake state. Additionally, a small increase in the Pa latency of AER as related to subconscious awareness was observed by the authors. These findings support the suggestions made in previous sections that the auditory processing is an important indicator of the subconscious neural processing which is especially vital for evaluating the states bordering between conscious awareness and sub consciousness like that of anesthesia awareness.

Conclusion

From the discussion above, it seems that auditory conscious awareness during anesthesia is not limited to overt conscious experiences. Instead, it involves a series of subconscious-unconscious responses of human mind including implicit recall and dreams. Both these conscious and unconscious processing contribute to anesthesia awareness experiences and their aftermath. From this view point, presently only MLAERs seem to have the potential to assess both these conscious and subconscious processes. However, they remain to be used more and developed more for subconscious awareness monitoring. Most importantly, their use should become more universal so that we can prevent cases of AA which are perhaps the most distressing adverse effects of anesthesia.

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