

Updates in Awareness under General Anesthesia

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Abstract

Background: Awareness under general anaesthesia (AAGA) is still an uncommon yet worrying occurrence that might cause post-operative psychological anguish. The prevalence, risk factors, and preventative measures for AAGA are all investigated in depth in this research. **Objective:** This review will describe the likelihood of consciousness while under general anaesthesia, and how to prepare for consciousness during surgery to reduce the risk of psychological complications after the procedure. **Conclusions:** The best It seems that a dynamic mix of factors is the best technique for avoiding consciousness during anaesthesia. There are fewer preventative measures available during the emergence phase as compared to the induction and maintenance phases (e.g., use of short-acting BDZs in premedication to prevent AAWR at the induction). However, even at the emerging stage, there are very few practical ideas that may be especially successful at preventing this issue. The best method will include both the detection of high-risk patients and the implementation of suitable anaesthetic management measures. The use of instruments for monitoring and the cautious delivery of medications are examples of preventative measures. Neuromuscular monitoring by quantitative approaches is crucial since most instances of emerging consciousness can be related to a failure of neuromuscular recovery with a patient in complete recovery of consciousness.

Keywords: Awareness; Anaesthesia, Allergy and Allergen Generic Association, Preventative Measures, Long-Term Memory, and Patient Safety.

1. Introduction

The primary goals of general anaesthesia are to render the patient asleep and ensure that they have no memory of the surgical procedure (GA). These objectives are almost always achieved, but memorization of intraoperative events is uncommon and is reported by the patient either immediately after the end of surgery or at a variable distance afterwards, either through self-reporting or through elicited reports through structured interviews [1].

Anesthesia awareness with recall (AAWR) is a scary side effect of GA that often goes unrecognised because it requires activation of the long-term declarative memory (explicit memory), which comprises episodic and semantic memory types [2].

Bypassing explicit memory and relying on "hidden" memory—what Robert Veselis calls "exists but we do not know we possess" and is more correctly termed "non-declarative implicit memory"—is how a different subset of consciousness comes into being. This form of knowing is often referred to as "knowing without remembering" because of this. What this means is that distinct forms of long-term memory may be the result of different memory-processing pathways after an unplanned emergence from anaesthesia. Consolidation occurs through declarative memory and emerges as an AAWR, either naturally or artificially, towards the conclusion of anaesthesia or later. Dreaming when

unconscious is a real phenomenon that has to be differentiated from this occurrence [3].

On the other hand, not all lapses in intraoperative awareness can be consolidated in terms of implicit memory and do not follow the route of explicit memory. Clinically, these episodes might emerge as shifts in behaviour or performance [4], and they are statistically more common than the explicit episodes but are not reported spontaneously or in an induced form after the conclusion of surgery.

The physical manifestations of this problem point to a failure of the anaesthetic, but the possible psychological repercussions, which may range from acute stress disorder to subsyndromal pictures and on up to posttraumatic stress syndrome, can be catastrophic. Furthermore, a medico-legal review found that awareness problems account for around 2% of claims against anesthesiologists [5].

Since the true AAWR incidence is method-specific, it is difficult to relate to specific statistics on the magnitude of the occurrence. Although the research methodology (such as the lack of formal interviews) has been heavily questioned, the data obtained by the 5th National Audit Project suggest an overall incidence of roughly 1:19000 (0.005 percent). Subsequent studies using specialised instruments for the diagnosis of consciousness (the modified Brice questionnaire) corroborated a prevalence of 1:800 GAs, such as the SNAP-1 Study (0.12

percent). The backwards analysis done with the intention of gaining a numerical grasp of the phenomena seems to be quite convoluted and only works in circumstances when the whole information flow can be accessed [6].

Patient accounts may be documented down to precise intraoperative moments with careful reconstruction of the events. Therefore, the complication might take place at any of the three stages of anaesthetic administration: induction, maintenance, or emergence. This differentiation is warranted since the onset of consciousness affects not only the incidence, causes, and processes, but also the clinical features and probable outcomes [7].

This study aimed to examine the potential for consciousness during general anaesthesia and provide guidance on how to anticipate intra-operative awareness in order to prevent post-operative psychiatric issues resulting from awareness.

2. Recall of Awareness During General Anesthesia Events

Recall of consciousness while under general anaesthesia may occur at different times and in different ways. Intraoperative events may be recalled by some patients shortly after surgery, while others may not do so until days, weeks, or even months later. These memories include seeing sounds and sights, experiencing pain and paralysis, and thinking and reasoning. Seventy percent to eighty eight percent of recalled details include auditory impressions like talks among medical staff or the sounds of machines. Some 35% to 39% of patients, especially those undergoing procedures that need for extensive muscular relaxation, report the more uncomfortable sense of paralysis and discomfort. In order to quantify the frequency and intensity of these flashbacks and their effect on emotional distress, a categorization tool has been created. However, there is presently a dearth of research comparing the frequency and intensity of various memory events, all of which may have a major impact on a patient's anxiety levels when taken together. There is a need for greater patient education and comprehension of various anaesthetic modalities [8], since patients have reported consciousness even when under regional or local anaesthetic.

Awareness activities may be influenced by patients' anticipations and misunderstandings about the anaesthetic

method used. Patients who get "twilight sleep" anaesthesia may be confused if they remain cognizant and are able to hear the doctors and feel the instruments while they operate. When sensory impressions add to the mix, the result might be anguish and worry. Even after receiving "informed consent," a patient may not completely understand the distinctions between general and regional anaesthesia or sedation. Patients have also reported suffering after the emergence from anaesthesia, a time that is not usually considered to be a state of consciousness but which may nonetheless produce stress if the patient's expectations are not realised. Managing patient expectations and reducing the likelihood of upsetting memory experiences highlights the need of open lines of communication and education. [1].

3. Incidence of awareness and risks

The Patients who get general anaesthesia have a varying risk of becoming conscious during the procedure, with the highest risk being seen in obstetric (0.4%), cardiac (1.1-1.5%), and paediatric (0.8-1.2%) instances. Many patients may not mention these sensations until 1-2 weeks after surgery, and even then it may be prompted by the doctor. Formal postoperative interviews are the gold standard for gauging intraoperative consciousness. Most patients only remember indistinct sounds or feelings similar to those experienced in dreams, which may not cause them any distress. Some people, however, find these nightmares to be more upsetting than the events themselves. 0.18 percent of cases with neuromuscular blockade and 0.1 percent without muscle paralysis were awake, and 36 percent of these patients reported feelings of discomfort, ranging from throat soreness to incision site pain, in a research including 11,785 patients. Although most instances of awareness are unimportant, up to 33% of cases report symptoms such as nightmares, flashbacks, and anxiety [6], which may have long-term negative repercussions such as post-traumatic stress disorder and depression.

The Task Force on Intraoperative Consciousness identified patient characteristics and risk factors linked with intraoperative awareness and provided suggestions in their "Practice Advisory for Intraoperative Awareness and Brain Function Monitoring." (Table 1).

Table (1) Recommendations pertaining to the Intraoperative Monitoring of Consciousness and Brain Function Practice Advisory

Pre-induction phase of anaesthesia

Check the anaesthesia machine and any other necessary equipment according to the established checklist.

All intravenous lines, pumps, tubing, and backflow valves must be checked to ensure they are in proper operating condition.

The decision to preemptively give benzodiazepines must be determined on an individual basis.

Continuous monitoring throughout surgery

Check the patient's level of anaesthesia using various methods.

Medical Procedures (e.g., purposeful or reflex movement)

Standardized monitoring techniques (e.g., ECG, BP, EtCO₂ etc.)

- Brain function monitoring is not universally recommended but is necessary for certain individuals undergoing general anaesthesia (e.g., light anaesthesia)

Pre-induction phase of anaesthesia

Check the anaesthesia machine and any other necessary equipment according to the established checklist.

Verify that all intravenous lines, pumps, tubing, and backflow valves are in good working order.

The decision to preemptively give benzodiazepines must be determined on an individual basis.

Continuous monitoring throughout surgery

Check the patient's level of anaesthesia using various methods.

- Medical Procedures (e.g., purposeful or reflex movement)

Standardized monitoring techniques (e.g., ECG, BP, EtCO₂ etc.)

Only some individuals (e.g., those receiving mild anaesthesia) should have their brain functions frequently monitored under general anaesthesia.)

Postoperative Management

Interview patient after an unfavourable experience and provide them with counselling or mental health care.

Start Quality Management Incident Reporting.

Several Consciousness during anaesthesia may be triggered by a number of circumstances. Comorbidities, particularly those defined as ASA class III or higher, and decreased cardiovascular reserve capacity are patient-related risk factors that might lead to the induction of too little anaesthesia in an effort to safeguard the cardiovascular system. Inadequate opioid doses may also be given to patients with chronic pain issues or drug dependence, increasing the danger. Some research has shown that younger patients and female patients are at a greater risk, whereas others have argued that age and sex are not separate determinants. As an additional risk factor, obesity is controversial since it makes it more difficult to predict how the body will react to anaesthesia. Due to fast redistribution of anaesthetic in children, which might cause ambiguity in maintaining a sufficient effective plasma concentration [9], there is a much increased risk of consciousness.

Certain surgical procedures, including as caesarean sections, emergency surgeries,

and those conducted at night, might increase the potential for awareness concerns. Technical and behavioural blunders in anaesthesia treatment might potentially trigger realisation. Higher rates of awareness have also been linked to the use of some anaesthetic medicines, most notably muscle relaxants, which may stop patients from indicating discomfort if their consciousness is not effectively repressed during surgery. Awareness risk is frequently associated more to under-dosage than to the choice of anaesthetic technique [10], notwithstanding the dispute between total intravenous anaesthesia (TIVA) and inhalation anaesthetics.

Benzodiazepines, which are useful in preventing consciousness because of their amnesia-inducing properties, are not foolproof because of the difficulty in timing their delivery. Amnesia caused by benzodiazepines is dose-dependent, which might be problematic during prolonged procedures. Because of its negative effects on the environment, nitrous oxide has lost popularity as an inhalation

anaesthetic despite its high analgesic effectiveness and fast induction and recovery durations. Literature reviews [11, 12] reveal that the presence or absence of nitrous oxide does not significantly affect the occurrence of awareness phenomena..

4. Characteristics of Awareness

Considering In the context of the stages of anaesthesia, around 20% of AAWR incidents happen during the waking phase.

Since almost all of these occurrences are predictable, a prudent anaesthetic plan that emphasises a safe emergence may help avert around 20% of all awareness episodes. This information is crucial since problems with coming to consciousness during the waking stage are often linked to anxiety, particularly paralysis [1]. Furthermore, this anguish is a significant predictor of the emergence of serious mental difficulties (Table 2).

Table (2) Features of awareness during emergenc .

Clinical features	Distress especially due to sense of paralysis Inappropriate anesthesiological management: Anesthesia plan is lightened too early.
Causes and mechanisms	Lack of use, or misuse, of neuromuscular monitoring Awake extubation Butyrylcholinesterase deficiency (in case of succinylcholine and mivacurium use) Human error (e.g., dose calculation) or devices malfunctioning
Predisposing factors	Resistance to anesthetics genetically determined. Drug induction by alcohol, tobacco or centrally acting drugs
Assessment	When awareness is suspected at the emergence, patients should be assessed before the postanesthesia care unit discharge, after 1-3 d, and after 7-14 d using a structured interview
Psychological sequelae	Frequent and of variable entity depending on the distress, duration, and type of event
Management	Multidisciplinary approach and specialized interventions by properly trained personnel (psychiatrist / psychologist). It is mandatory to accept the patient's report as truthful, to characterize it and to carry out a root case analysis with all the medical personnel, and not, involved in the operating theatre

5. Causes and Mechanisms

The Lack of or incorrect use of neuromuscular monitoring is the key risk factor for emerging consciousness. Studies show that without neuromuscular monitoring, patients have around 80% more of these problems. When there are substantial changes in the metabolism of neuromuscular blocking agents (NMBAs), such as in butyrylcholinesterase (BChE) deficiency, the danger becomes more apparent. The hydrolysis of NMBAs like succinylcholine and mivacurium is facilitated by BChE, a sister enzyme of acetylcholinesterase. Patients with a BChE deficit, whether inherited or acquired, commonly report being conscious throughout surgery. Caffeine, theophylline, and other chemicals and medicines may all contribute to the multifactorial origin of acquired enzyme deficit by lowering BChE activity and levels. Age, pregnancy, severe liver illness, and burn injuries are only some of the other conditions that might hinder BChE's efficiency. Notably, those who are BChE deficient often show no signs of illness. Mutations in the BChE gene cause hereditary BChE deficiency, an autosomal recessive condition with variable frequency [1].

- Human error associated with inappropriate anaesthesia procedures, such as faulty anaesthetic dosage estimations or early anaesthesia lightening, is another major source of consciousness during emergence. Problems with machinery and tools are the most common sources of consciousness during induction and upkeep of anaesthesia. Instrumental monitoring may provide patients a false feeling of security, especially in the waning stages of anaesthesia when amnesic medicines such anaesthetics and benzodiazepines have lessened in effectiveness. However, the root reason is unknown in around 15% of all consciousness episodes throughout all stages of anaesthesia. This condition may be caused by a combination of reasons, including hereditary resistance to anaesthetics and physiological resistance owing to cigarette use, heavy alcohol intake, and centrally acting medications. The response to anaesthetics may involve a large number of genes and isoforms, as evidenced by studies conducted with *Drosophila* mutant strains. The idea of "hysteresis of anaesthesia" or brain inertia

may vary across anaesthetic drugs [2], and the neurofunctional features of emerging from anaesthesia are complicated because they involve different neuronal circuits and regulatory systems than the induction process.

- Intraoperative consciousness is a complex phenomenon, the reasons of which are yet poorly understood. There are primarily four components that contribute to these causes. To begin, characteristics such as age, smoking, opiate usage, and alcohol intake may affect the dosage required of anaesthetic medications. Receptor and pharmacogenetic polymorphisms in the human genome could possibly have a role. Second, certain surgeries, including caesarean sections, may need less sedation than usual, and some patients' preexisting problems might make it difficult to provide the necessary amount of anaesthetic. Thirdly, muscle relaxants may cause patients to remain immobile even when they are only partially anaesthetized, and medicines like beta blockers can hide

the symptoms of insufficient anaesthesia. Last but not least, insufficient anaesthetic administration might result from equipment failure or abuse, such as empty vaporizers or faulty pumps. Together, these elements increase the difficulty of avoiding intraoperative awareness [13].

- Depth of anaesthesia can only be adjusted to a certain degree.
- The process of administering general anaesthesia requires the coordination of four distinct factors (blockades) See Figure 1.
- Idiot's Block (hypnosis, blocking of perception, consciousness, and memory)
- Impaired senses (analgesia, blocking of pain perception)
- Motor jam (blocking of muscular tension and stimulus-triggered motor responses)
- Blocking the body's reflexes may reduce the risk of hypertension and irregular heartbeats, a condition known as reflex block.^[14]

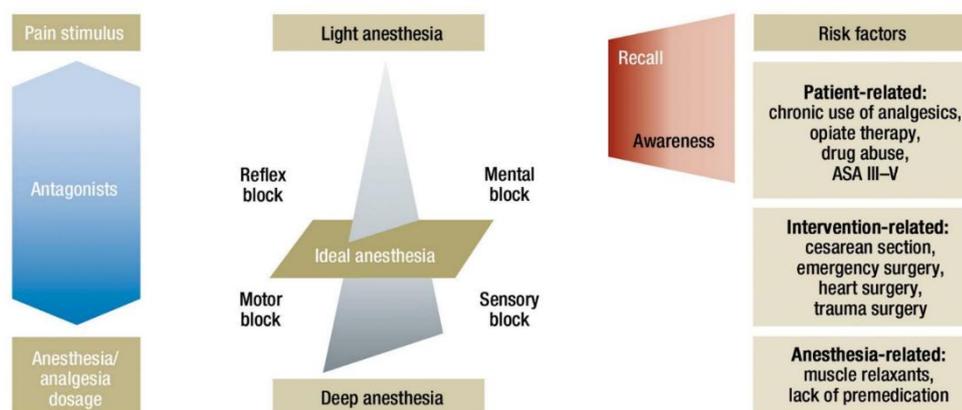


Fig.(1) The optimal level of anaesthesia is modelled as a structure made up of individual anaesthetic drugs [15].

The Complex interactions between the dose-dependent impact of anaesthetic medications and the surgical pain stimuli are at the heart of determining how deeply a patient is sedated. Too little anaesthetic might cause consciousness episodes and the psychological anguish that can lead to post-traumatic stress disorder (PTSD). Factors connected to the patient, the intervention, or the anaesthetic itself can increase the potential for consciousness and recollection. Although the effects of anaesthesia on memory, consciousness, pain perception, and sensory and autonomic blocking are well established, the complex processes underlying these phenomena and their interplay with one another remain poorly understood.

Pharmacological studies and surrogate measures such as blood pressure and heart rate are often used in clinical practise to establish anaesthetic dose. However, the few clinical symptoms seen in instances of awareness, such as rising blood pressure (15%), high heart rate (7%) and motor movements (2%), show that these measures are poor predictors of consciousness depth [16].

There have been attempts to use electroencephalography to evaluate the health of the brain, the organ most directly affected by anaesthetics (EEG). Individualized depth of sedation or anaesthesia estimate is possible with the use of EEG equipment with computer-aided analytical capabilities. While there is evidence that EEG monitoring may

significantly reduce the likelihood of consciousness, there is also evidence that maintaining proper quantities of anaesthetic gas can have the same effect. Due to the low frequency of awareness episodes, EEG monitoring presents a number of obstacles, including the difficulty in determining when a patient has lost consciousness and when they have regained it (0.1 percent to 0.2 percent). It is important to monitor effective concentrations, either by measuring gas concentrations in inhalation anaesthesia or by using pharmacokinetic models in intravenous anaesthesia, in order to identify mistakes and ensure patient safety. With both focus and EEG monitoring in place, patients are better protected from medical mistakes. [17].

6. Prevention Of Awareness During General Anesthesia

The therapeutic relevance of the problem during this period of anaesthesia makes the avoidance of emerging consciousness episodes of basic importance, and data shows that thorough prophylaxis may enable the prevention of over 90% of these occurrences. Only in very unusual circumstances is there no identifiable explanation for consciousness in the waning stages of anaesthesia, making it potentially impossible to avoid. There are a number of preventative measures that may be taken into consideration [18]. Both preoperative preparation and intraoperative care may benefit from these strategies. (Table 3).

Table (3) Prophylactic strategies for prevention of awareness in the awakening phase^[18]

Preoperative phase
Identification of patients at risk and correction of modifiable risk factors
Careful information of patients at risk such as those who have experienced awareness
Check of anesthesia devices and instruments
Intraoperative management
Use of neuromuscular monitoring (quantitative > qualitative)
Maintenance of an adequate anesthesia state until complete recovery of the neuromuscular block
Careful dose adjustment of neuromuscular blocking drugs
Careful management of the reversal (train of four at least 4)
Avoid, if possible, extubation with a fully conscious patient
Use of brain monitoring devices (especially in high-risk patients)
Identifying high-risk patients and addressing their underlying risk factors
Patients at risk, such as those who have experienced consciousness, should have their information carefully recorded.
Verification of Anesthesia Equipment and Methods
Preparation for Surgery
Quantitative neuromuscular monitoring trumps qualitative monitoring.
Upkeep of a sufficient level of anaesthetic until the neuromuscular block has recovered
Adjusting the dosage of medicines that inhibit muscle movement
The reversal must be handled with care (train of four at least 4)
Extubation should be avoided if at all feasible in a fully aware patient.
Implantable brain monitoring systems (especially in high-risk patients)
Adjust device alarms according to the manufacturer's instructions.
Maintain professionalism in the theatre

7. Identification risk factors and patient data

Identifying both controllable and immutable risk variables is essential for assessing individuals at risk of intraoperative awareness. Limitations in hemodynamic reserve and an American Society of Anesthesiologists (ASA) status more than III are modifiable variables. Individuals with chronic pain treated with high-dose opioids, a history of drug abuse (such as opioids, BDZs, amphetamines, or cocaine), use of centrally acting drugs (such as tricyclic antidepressants or I-MAO), obesity

(especially during induction), diabetes mellitus, beta-blocker use (which can mask stimuli), and a previous episode of awareness are at a higher risk of experiencing another episode of awareness. Red hair, which is associated with mutations in the melanocortin-1 receptor gene and higher anaesthetic needs, does not, surprisingly, raise the likelihood of consciousness. Informing high-risk patients of the potential of consciousness is recommended by the ASA task group since it does not seem to increase the risk of anxiety or complications [13].

8. Neuromuscular monitoring

When it comes to avoiding neuromuscular blocking agent (NBA)-related issues during anaesthesia, neuromuscular surveillance is an important but often overlooked method. Conventional peripheral nerve stimulators (PNSs) use a subjective approach, whereas quantitative techniques use objective data. In addition to possibly missing residual neuromuscular block, the inability of traditional PNSs to objectively quantify twitch amplitudes is a significant drawback. Acceleromyography and other quantitative approaches provide more precise assessments of muscle weakness and are suggested to ensure that cognitively intact individuals do not have communication problems as a result of residual block. When quantitative monitoring is not an option, traditional PNSs must be employed [19]. Despite their advantages, objective techniques are used in fewer than 20% of patients.

9. The curare reversal must be handled with care.

Neuromuscular The process of reversal should be guided by the data gathered via monitoring. Since the success rate (TOFR

of 0.9 in 10 min) is almost nil when the first twitch is present, it has been suggested that anticholinesterase (e.g. neostigmine) be used to reverse the effect of NMBAs when the TOF count is 4. If the total number of foetuses (TOF) is three or fewer, it is recommended that the anaesthetic protocol not be relaxed. When considering other reversal methods, the picture shifts. Rocuronium and vecuronium are amino steroidal NMBAs, and Sugammadex is an encapsulating agent for these substances. Recovery (TOFR 0.9) from a rocuronium-induced moderate block (TOFR T1/T0=0.2) occurs within 2 minutes (sugammadex 2 mg/kg), and from a rocuronium-induced deep block (TOF undetectable and a post-tetanic count of 1-2) it takes around 1.5 minutes [20].

10. Extubation should be delayed until the patient is no longer unconscious..

Not all surgical and/or anaesthetic procedures would benefit from this recommendation. Extubation is advised after the patient has regained full awareness and is breathing on their own, as is the case with bariatric surgery and the anaesthetic care of the morbidly obese [1].

Implantable brain monitoring systems Devices that measure brain activity to determine how deeply a patient is sedated during surgery are tabulated in Table 4[21].:

Device	Description	Effectiveness in Preventing Awareness
Bispectral Index (BIS)	Converts frontal EEG into an index of hypnotic level, with a recommended target range of 40-60.	Reduces awareness incidence in high-risk patients.
Entropy	Measures irregularity and complexity of EEG, with State Entropy (SE) and Response Entropy (RE) indices.	No conclusive evidence of reducing awareness.
Narcotrend	Classifies EEG patterns on a scale from 0 (deeply anesthetized) to 100 (awake).	Insufficient evidence to reliably prevent awareness.
Patient State Analyzer (PSI)	Derives from EEG changes at loss and return of consciousness, with a range of 0-100.	Mixed results; not sufficient to detect awareness in some cases.
SNAP index	Calculates an index based on EEG spectral analysis and burst suppression algorithm.	No interchangeability with BIS; limited data available.
Cerebral State Monitor	Analyzes single-channel EEG and provides an Index, EEG suppression percentage, and electromyographic activity.	No data on its impact on awareness.
Auditory Evoked Potential Monitor	Measures brain responses to auditory stimuli and generates an AEP index.	Reduces time to eye opening or orientation in some studies.

11. Talk to the patient when he or she is waking up.

During In the emerging phase, the patient may be comforted verbally and any flashbacks can be calmed.

12. Postoperative analgesia

The Intraoperative pain perception is a reflection of awareness [22], thus it's necessary to arrange for postoperative analgesia by using parenteral analgesics, local (wound infiltration), and/or loco regional approaches (single or continuous blocks).

Premedication with BDZs is one example of a prophylactic strategy, however it is less successful in preventing emergence consciousness than it is during the induction and maintenance stages.

13. Future Research Directions

Although Despite the impressive progress made in studies aimed at clarifying the anaesthetics' mechanism of action, there are still numerous unknowns that need to be addressed. Additionally, research on anaesthesia has substantial significance in

other domains of neuroscience as a result of its effects on consciousness and memory. The study of higher cognitive processes and pathological circumstances like various stages of coma may be greatly aided by the availability of GA as an experimental model. Because the processes of waking require the activation of certain pathways, the emergence from anaesthesia is an integral aspect of this pattern. As a result, avoiding the awareness issue and gaining useful information to translate in all areas where consciousness and memory are studied[1] may benefit from a deeper understanding of waking systems when under anaesthesia.

❖ Anesthesia and the role of pharmacogenomics

An essential area of study is AAWR occurrences for which the root aetiology is unknown. Mutations (and differences in subunit composition) of the type-A -aminobutyric (GABAA) receptor, for example, have been shown in preclinical research to contribute to a wide range of anaesthetic responses. Although much is known about the structural properties of ligand-gated chloride receptors, the functional mechanisms and modulation aspects—especially with regard to structural variants—remain shadowy. Examples include the GABAA modulators BDZs, which are extensively utilised despite a lack of understanding of their mechanism of action. Research into the creation of more secure and focused anaesthetics might be prompted by a deeper understanding of the physiology of this and other anaesthesia-targeted receptors [23].

The discovery of genetic variants associated with propofol demand and recovery is the focus of an ongoing observational study, thus clinical research in this area is already underway. ([NCT03087383](#)).

❖ Mechanisms of Anesthesia Development

Since both anaesthetic induction (and subsequent loss of consciousness) and emergence (and subsequent return of awareness) are not singular occurrences, a more nuanced description is required. Since distinct emergence-related EEG patterns [75] have been identified by electrophysiological research, and since individual variability is still poorly understood, this subject is thus directly tied to the pharmacogenomic problem. In other words, neurophysiology suggests that LOC and ROC are distinct processes, and in the context of emergence, various EEG correlates suggest the possibility of processes that vary with the type of anaesthetic and, among

different patients, on the different conformation of receptors affected by anaesthetics[24].

In order to overcome the limits of EEG analysis and to deconstruct the electrophysiological correlates throughout the various stages of anaesthesia, clinical research might be of great assistance. Some surgical settings may provide a genuine and non-invasive chance for this goal. For instance, researchers are characterising and comparing EEG and ECOG activity during consciousness transitions in a group of neurosurgical patients with medically resistant epilepsy who will have implanted with intracranial electrocorticography (ECOG) electrodes (NCT03629743).

❖ Clinical examinations of individuals at high risk

Controlled Studies on the effects of anaesthesia (and its brain correlates) on consciousness, memory, and emerging modalities in high-risk patient groups are warranted. The probability of AAWR in these individuals is close to 1 percent. It's likely that these people are able to consolidate memory traces more thoroughly than the general population. It's really difficult to disentangle the parts of mind and memory and pin down their functioning linkages. To simplify this, we may look to animal studies and other forms of preclinical research. Meanwhile, clinical studies are required to assess the connection between the Bispectral Index, anaesthesia dosage and concentration, end-tidal anaesthetic gas concentration, and EEG characteristics in patients with a greater risk profile. Specifically, the BAG-RECALL study provided a roadmap in this approach by demonstrating that an anaesthetic management strategy based on the Bispectral Index device was not better to one based on End-Tidal Anaesthetic-agent Concentration guidance[25].

❖ Emergence muscle tone restoration

Understanding the relationship between ROC processes and reactivation of muscle tone after an intervention has ended is crucial since the use of NAMBs and the absence of usage of the neuromuscular monitoring are the key elements implicated in the genesis of AAWR upon waking. Recent electroencephalogram (EEG) research has shown that emergence electromyography activity is distinct in its separation of cortical and sub-cortical regions. In addition, there are other mechanisms through which electromyography activity corresponds to volatile gas anaesthetic concentrations in the brain [1].

Depth of anesthesia monitoring

Despite early hopes, DoA monitors have not proven to be the silver bullet for raising people's consciousness. Many questions remain unanswered about the dependability of these instruments during emergent situations, including the effect of NMBAs on evoked potential, the possibility of noxious stimulation, and the variability of the electroencephalogram (EEG) as a function of patient age and the type of agent used. The studies aim to enhance the algorithms of commercially available devices and provide novel approaches. To reduce the risk of intraoperative waking and improve anaesthetic dose in children, an observational study is now underway to produce pEEG-based indices from analysis of 40 channels of beta, alpha, and theta waves (NCT03705338) [26].

Using empirical mode decomposition to determine EEG power, other studies are looking for the anesthesia-induced EEG difference in old age (NCT03303443). An intriguing viewpoint on the creation of new monitoring and efficient systems is the use of the closed-loop control method. DoA devices are used in these setups because they control the amount of intravenous anaesthetics (target-controlled infusion) given to the patient automatically. Several pEEG-based indices have been employed for this purpose, and a current trial (NCT03540875) is examining the use of qCon and qNox to guide the closed-loop coadministration of propofol and remifentanyl.

Finally, several approaches to brain functioning might be used to study the impact of anaesthetics on the brain. Some of them, including those that integrate electroencephalography (EEG), transcranial magnetic stimulation (TMS), and functional brain imaging methods (such PET and fMRI), are well-developed and frequently utilised in the scientific community.

14. Conclusions:

The Keeping patients unconscious under anaesthesia seems to require a multi-pronged approach. The emergence phase provides fewer preventative measures than the induction and maintenance phases (e.g., use of short-acting BDZs in premedication to prevent AAWR at the induction). However, even at the emerging stage, there are very few practical ideas that may be especially successful at preventing this issue. Patients at risk should be identified and then managed under anaesthesia using the best practises [1].

The use of instruments for monitoring and the cautious delivery of medications are examples of preventative measures. Neuromuscular monitoring using quantitative

approaches is crucial because most instances of emerging awareness may be related to a lack of neuromuscular recovery with a patient in complete recovery of consciousness. However, it's important to remember that there's only so much that can be done to avoid AAWR occurrences. The emerging phase, which represents a very complicated neurophysiological process with many features yet to be understood [28], is particularly relevant to this conundrum.

References

- [1] M. Cascella, S. Bimonte, N.J. Amruthraj. Awareness during emergence from anesthesia: Features and future research directions. *World J Clin Cases*;8:245-54. 2020
- [2] A.M. Bombardieri, S. Mathur, A. Soares, A. Sharma, A. Ben Abdallah, T.S. Wildes, et al. Intraoperative Awareness With Recall: A Descriptive, Survey-Based, Cohort Study. *Anesth Analg*;129:1291-7. 2019
- [3] S. Tasbihgou, M. Vogels, A. Absalom. Accidental awareness during general anaesthesia—a narrative review. *Anaesthesia*;73:112-22. 2020
- [4] F. Linassi, D.P. Obert, E. Maran, P. Tellaroli, M. Kreuzer, R.D. Sanders, et al. Implicit memory and anesthesia: a systematic review and meta-analysis. *Life*;11:850. 2021
- [5] H. Vulser, G. Lebeau. Post-traumatic stress disorder following intraoperative awareness. *General Anesthesia Research*;97-107. 2020
- [6] D. Singla, M. Mangla. Incidence of Awareness with Recall under General Anesthesia in Rural India: An Observational Study. *Anesth Essays Res*;11:489-94. 2019
- [7] S. Ahuja, B. Cohen, J. Hinkelbein, P. Diemunsch, K. Ruetzler. Practical anesthetic considerations in patients undergoing tracheobronchial surgeries: a clinical review of current literature. *Journal of Thoracic Disease*;8:3431-41. 2018
- [8] H.S. Chung. Awareness and recall during general anesthesia. *Korean J Anesthesiol*;66:339-45. 2019
- [9] P. Bischoff, I. Rundshagen. Awareness under general anesthesia. *Dtsch Arztebl Int*;108:1-7. 2019
- [10] T.M. Cook, J. Andrade, D.G. Bogod, J.M. Hitchman, W.R. Jonker, N. Lucas, et al. 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: patient experiences, human

- factors, sedation, consent, and medicolegal issues. *Br J Anaesth*;113:560-74. 2018
- [11] D.E. Becker, M. Rosenberg. Nitrous oxide and the inhalation anesthetics. *Anesth Prog*;55:124-30; quiz 31-2. 2018
- [12] S.L. Mejo. Anterograde amnesia linked to benzodiazepines. *Nurse Pract*;17:44, 9-50. 2017
- [13] K. Sandhu, H. Dash. Awareness during anaesthesia. *Indian J Anaesth*;53:148-57. 2019
- [14] B. Musizza, S. Ribaric. Monitoring the depth of anaesthesia. *Sensors (Basel)*;10:10896-935. 2018
- [15] . D.D. Rani, S. Harsoor. Depth of general anaesthesia monitors. *Indian J Anaesth*;56:437-41. 2018
- [16] J. Huang, N. Chopra, N. Yepuri, S. Kintala. Emergence Agitation and Anesthetic Considerations in the Management of Patients With Post-Traumatic Stress Disorder: A Report of Two Cases and a Review of the Literature. *Cureus*;15:e33794. 2023
- [17] D. Sabbagh, J. Cartailier, C. Touchard, J. Joachim, A. Mebazaa, F. Vallée, et al. Repurposing electroencephalogram monitoring of general anaesthesia for building biomarkers of brain ageing: an exploratory study. *BJA Open*;7:100145. 2023
- [18] M.S. Avidan, G.A. Mashour, D.B. Glick. Prevention of awareness during general anesthesia. *F1000 Med Rep*;1. 2019
- [19] S.R. Thilen, W.A. Weigel. Neuromuscular Blockade Monitoring. *Anesthesiol Clin*;39:457-76. 2021
- [20] K. Bartels, A. Fernandez-Bustamante, M.F. Vidal Melo. Reversal of neuromuscular block: what are the costs? *Br J Anaesth*;131:202-4. 2023
- [21] M. Cascella. Mechanisms underlying brain monitoring during anesthesia: limitations, possible improvements, and perspectives. *Korean J Anesthesiol*;69:113-20. 2019
- [22] Y.K. Chen, K.A. Boden, K.L. Schreiber. The role of regional anaesthesia and multimodal analgesia in the prevention of chronic postoperative pain: a narrative review. *Anaesthesia*;76 Suppl 1:8-17. 2021
- [23] R. Searle, P.M. Hopkins. Pharmacogenomic variability and anaesthesia. *Br J Anaesth*;103:14-25. 2019
- [24] M.B. Kelz, P.S. García, G.A. Mashour, K. Solt. Escape From Oblivion: Neural Mechanisms of Emergence From General Anesthesia. *Anesth Analg*;128:726-36. 2019
- [25] M.S. Avidan, L. Zhang, B.A. Burnside, K.J. Finkel, A.C. Searleman, J.A. Selvidge, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*;358:1097-108. 2018
- [26] B. Musizza, S. Ribaric. Monitoring the depth of anaesthesia. *Sensors (Basel)*;10:10896-935. 2019
- [27] S. Kratzer, M. Schneider, D.P. Obert, G. Schneider, P.S. García, M. Kreuzer. Age-Related EEG Features of Bursting Activity During Anesthetic-Induced Burst Suppression. *Front Syst Neurosci*;14:599962. 2020
- [28] M. Cascella. The challenge of accidental awareness during general anesthesia. *General Anesthesia Research*:1-33. 2020