Subjective Experiences under Dexmedetomidine and Propofol Induced Unresponsiveness

Milla Karvonen, 36631
Pro gradu-avhandling i psykologi
Handledare: Katja Valli
Petra Grönholm-Nyman
Fakulteten för humaniora, psykologi och teologi
Åbo Akademi
2017

ÅBO AKADEMI – FAKULTETEN FÖR HUMANIORA, PSYKOLOGI OCH TEOLOGI

Abstrakt för avhandling pro gradu

Ämne: Psykologi	
Författare: Milla Karvonen	
Arbetets titel: Subjective Experiences under Dexmedetomidine and Propofol Induced Unresponsiveness	
Handledare: Katja Valli	Handledare: Petra Grönholm-Nyman

Abstrakt:

The aim of the present study was to explore subjective experiences in healthy young participants undergoing anesthesia in a nonsurgical, purely experimental setting. Studies conducted in surgical settings have shown that subjective experiences are sometimes reported after anesthesia despite the seeming unresponsiveness of the patients during the surgery. Anesthesia awareness and dreaming under anesthesia are examples of these anesthesia-related subjective experiences. In this study, participants were awakened during single-drug anesthetic infusion in order to better establish the timing and the nature of these experiences.

Forty-seven healthy male volunteers participated in the study. They were administered either of the two anesthetic agents, dexmedetomidine (*n* = 23) or propofol (*n* = 24). The anesthetic dose was increased stepwise until the participant became unresponsive, and eventually the dose was increased to 1.5 fold to obtain certain loss of consciousness. The participants were interviewed on their subjective experiences both during the anesthetic infusion and upon the emergence from anesthesia after a short recovery period. The interviews were then content analyzed by two independent judges using scales designed for investigating subjective experiences during anesthesia.

The participants anesthetized with dexmedetomidine were significantly more arousable during the anesthetic infusion than the participants receiving propofol, and thus more often interviewed. With both anesthetics, the majority of the successful awakenings during infusion led to a report that included subjective experiences. Upon the emergence from anesthesia after a recovery period, the dexmedetomidine participants reported significantly more anesthesia experiences than the propofol participants. Dream-like imagery was the most commonly reported subjective experience (84.9%) with both anesthetics, whereas awareness of the environment was rare and always linked to brief arousals.

This is the first study conducted in which participants have been interviewed during anesthetic infusion. The obtained reports indicate that the subjective experiences do not only originate from the recovery period following the termination of the drug infusion. Thus, despite rendering the individual unresponsive and disconnected from the environment, light experimental anesthesia does not necessarily induce unconsciousness, i.e. absence of subjective experiences.

Nyckelord: Contents of consciousness, unresponsiveness, subjective experiences, anesthesia awareness, anesthesia dreaming	
Datum:	Sidoantal: 58
Abstraktet godkänt som mognadsprov:	

ÅBO AKADEMI – FAKULTETEN FÖR HUMANIORA, PSYKOLOGI OCH TEOLOGI

Abstrakt för avhandling pro gradu

Ämne: Psykologi	
Författare: Milla Karvonen	
Arbetets titel: Subjektiva upplevelser vid anestesi som framkallats av dexmedetomidine eller propofol	
Handledare: Katja Valli	Handledare: Petra Grönholm-Nyman

Abstrakt:

Målsättningen med denna studie var att undersöka subjektiva upplevelser hos friska unga forskningsdeltagare som sövdes ned i ett rent experimentellt upplägg. Studier som genomförts i samband med kirurgiska operationer har påvisat att subjektiva upplevelser ibland rapporteras efter anestesin även om patienterna till synes varit oresponsiva under operationen. Medvetenhet vid anestesi (anesthesia awareness) och drömmande vid anestesi (anesthesia dreaming) är exempel på anestesirelaterade subjektiva upplevelser. I föreliggande studie väcktes deltagarna under anestesiperioden för att få en tydligare bild av de ovannämnda subjektiva upplevelsernas tidsmässiga förekomst och natur.
Fyrtiosju friska manliga forskningspersoner deltog i studien. Två olika anestesiläkemedel, närmare bestämt dexmedetomidine (*n*=23) eller propofol (*n*=24), administrerades till dem. Dosen av anestesiläkemedlet höjdes gradvis tills forskningspersonen uppnådde ett oresponsivt tillstånd, och senare höjdes dosen 1.5 gånger för att säkra förlust av medvetenhet. Forskningspersonen intervjuades om sina subjektiva upplevelser både under anestesiperioden och när de kommit ut ur anestesin efter en kort återhämtningsperiod. Intervjuernas innehåll analyserades sedan av två av varandra oberoende bedömare med hjälp av skalor som utvecklats speciellt för undersökning av subjektiva upplevelser vid anestesi.

Forskningspersonerna som var nedsövda med dexmedetomidine gick signifikant oftare att väcka under anestesiperioden, och därför intervjuades de även oftare jämfört med forskningspersonerna som fick propofol. Med båda anestesiläkemedlen ledde majoriteten av framgångsrika väckningar under anestesiperioden till en rapport som innefattade subjektiva upplevelser. Efter anestesin rapporterade forskningspersonerna som fått dexmedetomidine signifikant flera anestesiupplevelser än de som fått propofol. Drömliknande upplevelser var den mest rapporterade subjektiva upplevelsen (84.9%) vid båda anestesiläkemedlen, medan medvetenhet om omgivningen var ett sällsynt fenomen och alltid kopplat till korta uppvaknanden.

Detta är den första studien inom området, i vilken deltagarna har intervjuats under själva anestesiperioden. Resultaten visar att subjektiva upplevelser inte endast härstammar från återhämtningsperioden efter anestesin. Sammanfattningsvis kan konstateras att lätt experimentell anestesi inte nödvändigtvis medför omedvenhet, trots att individen är oresponsiv och inte är i kontakt med omgivningen.

Nyckelord: Contents of consciousness, unresponsiveness, subjective experiences, anesthesia awareness, anesthesia dreaming	
Datum:	Sidoantal: 58
Abstraktet godkänt som mognadsprov:	

Contents

Introduction

The study of consciousness has established itself as a modern scientific field in the last three decades (Revonsuo, 2010). There is currently a considerable drive to put the philosophical theories on consciousness to test with empirical experiments. The ultimate objective of these studies is to link subjective experiences and behavior with their neural counterparts. The definition of consciousness and its neurological and behavioral markers are at the core of this research. It has been shown that the relationship between the presence of consciousness and its outer markers, such as reactivity, is by no means a straightforward one (e.g. Owen et al., 2006). One example on this discrepancy is the subjective experiences patients occasionally report after surgeries performed under general anesthesia when they have been seemingly unconscious. Although patients undergoing general anesthesia do not react to their environment, they may experience dreaming. On rare occasions, they may even be aware of their surroundings and the actual operation at hand, and this phenomenon has been coined as *anesthesia awareness*.

The research on these anesthesia-related phenomena, anesthesia awareness and dreaming under anesthesia, contribute both to the consciousness studies as a field as well as to the clinical anesthesia practices. Although anesthesia awareness seems to be relatively infrequent, ranging from 0.10 to 0.14% (Mashour et al., 2012; Samuelsson, Brudin, & Sandin, 2008a; Sebel et al., 2004), dreaming under anesthesia seems to be more common and has been reported to vary between 21.4−25.5% (Stait, Leslie, & Bailey, 2008; Leslie, Skrzypek, Paech, Kurowski, & Whybrow, 2007; Brandner, Blagrove, McCallum, & Bromley, 1997). The analysis of the contents of anesthesia dreaming and awareness may offer some insights into the underlying anesthetic mechanisms in the brain as well as into the hypothesized connection between anesthesia and natural physiological sleep.

The major problem in anesthesia awareness and dreaming studies relates to the methodologies used. The length and the depth of anesthesia required for different medical interventions, the way in which the patients are interviewed about their experiences, and the delay between the recovery from anesthesia and the interview render the results questionable. Furthermore, the combination of various anesthetic agents and other drugs administered during surgery, such as pain medication and muscle relaxants, may affect memory and reduce recall for experiences that originate from the anesthesia period. In this study, we used a nonsurgical experimental setting where healthy young subjects were rendered unresponsive with light doses of two anesthetic agents, either propofol or dexmedetomidine. The participants were interviewed on their subjective experiences both during the anesthetic infusion by awakening the participants while keeping the drug dose constant and after a short recovery period following the termination of their anesthetic infusion, i.e. upon emergence from anesthesia. These interviews were then analyzed and categorized according to a coding system designed for the content analysis of anesthesia reports in order to find out how frequently the participants report subjective experiences during anesthetically induced unresponsiveness and what these experiences are like.

Consciousness, Connectedness and Responsiveness

Consciousness is a subjective experience (Tononi & Laureys, 2009) and has been defined as “what abandons us every night when we fall into dreamless sleep and returns the next morning when we wake up or when we dream” (Sanders, Tononi, Laureys, & Sleigh, 2012, p. 946). Consciousness can be understood, defined and categorized in many different ways and on many different levels within the neurocognitive and philosophical domains. From a neurocognitive perspective, Damasio and Meyer (2009), for example, make the division between *core consciousness* that is enabled by individual’s capacity to wakefulness, image-making and attention, and *extended consciousness* which is then further assisted by language, memory and reasoning skills. Block (1995) and Revonsuo (2010), in contrast, build their concept of *phenomenal consciousness* on subjective experience. Phenomenal consciousness refers to any subjective experience the individual has in any state of consciousness and does not necessarily include the ability to communicate this experience to the environment. Hence, the subjective experiences one has while sleeping or under general anesthesia are also included in the definition of phenomenal consciousness, and those contents may later be exposed to cognitive processing through reflective consciousness (Revonsuo, 2010).

There are also different attributes one can apply in relation to consciousness: *connected, disconnected and responsive* (Sanders et al. 2012). Consciousness can be connected to the environment allowing us to experience external stimuli, like in wakefulness, or disconnected from the environment, like during dreaming when we have internally generated subjective experiences that have no counterparts in the physical world. Responsiveness, in contrast, refers to our behavioral interactions with the physical world and is not necessarily straightforwardly coupled to either consciousness or connectedness. For example, dreaming individuals are largely unresponsive to their environment despite having conscious experiences and sleepwalkers are spontaneously responsive despite typically having no recall of any types of subjective experiences during the episode (Sanders et al., 2012). Furthermore, during anesthesia awareness the anesthetized patient is conscious and connected to the environment but unable to communicate this in any way, i.e. is unresponsive. During surgical anesthesia, responsiveness is typically inhibited by muscle relaxants, but postoperatively the patients may sometimes report dreaming, even anesthesia awareness, suggesting that they may have been conscious, even connected, during surgery. This phenomenon highlights the complex relationship between consciousness and its behavioral indicators and demonstrates that unresponsiveness as such cannot be considered a reliable indicator of unconsciousness or disconnectedness.

Despite numerous experimental efforts, the exact neural correlates of consciousness are still to a large part a mystery. The only solid conclusion that can be made is that the cortico-thalamic system seems to be of importance, since broad lesions induced to it result in unconsciousness whereas lesions to other parts of the brain do not (Tononi & Laureys, 2009). Due to this lack of knowledge, we cannot directly measure the presence or absence of subjective experiences in an unresponsive individual, and hence be sure whether they are conscious or not. For the moment, to gain information regarding the presence and specific content of subjective experiences, we have to rely on the individual's own retrospective accounts.

General Anesthesia

Etymologically anesthesia refers to the loss of the ability to experience sensations (Greek -an − 'without'; aisthēsis − 'sensation'). Suppressing the experience of surgery can indeed be considered the main aim of anesthesia, together with analgesia (pain relief) achieved with analgesic drugs and immobility achieved with muscle relaxants. This suppression of surgery experience can be attained either by rendering the patient unconscious or ensuring that they are disconnected from their environment (Sanders et al., 2012). This can be done with different anesthetic agents (i.e., anesthetics). Although the mechanisms by which the different anesthetics cause unconsciousness remain yet somewhat unclear, they seem to do it by suppressing cortical functioning, blocking arousal through thalamus and stopping the process of information integration within the thalamocortical system that seems to be, as stated above, crucial to consciousness (Alkire, 2009).

Anesthetics are divided into two categories: general anesthetics that induce a reversible loss of consciousness or responsiveness and local anesthetics that cause a reversible loss of sensation in a certain region of the body with no effect on consciousness or responsiveness. For the general anesthetics, there are two ways in which they can be administered, either intravenously or by inhalation (Alkire, 2009). In this study, two general anesthetic agents, propofol and dexmedetomidine, were administered intravenously in order to reach a state of unresponsiveness and these drugs are thus described further below.

Propofol is believed to work mainly through potentiation of gamma-aminobutyric $acid_A$ ($GABA_A$) receptor activity (e.g. Eaton et al., 2016). It is one of the most commonly used anesthetic agents and seems to have some unique effects on consciousness and responsiveness both neurologically and behaviorally. It appears to shut down some parts of the brain while allowing others that take part in creating consciousness to remain active. In a study by Boly et al. (2012), mild propofol sedation was associated with a relative increase in thalamic excitability, and thalamocortical connectivity was preserved even in unresponsive individuals. Another study showed that lower doses of propofol suppress purposeful responsiveness to external stimulation, while the subject still remains somewhat conscious, as measured by functional magnetic resonance imaging (fMRI)

(Mhuircheartaigh et al., 2010). It has also been shown that propofol disrupts the brain's ability to transfer information from lower-order sensory processing areas to higher-order areas (Liu et al., 2011). The difference in propofol's functional mechanisms compared to some other anesthetic agents has been suspected also because propofol-based anesthesia has been associated with a higher incidence of dreaming in many studies (Leslie & Skrzypek, 2007).

Dexmedetomidine is a relatively selective alpha2-adrenergic receptor agonist, and usually used as a sedative agent accompanied by other anesthetics during surgery. It most probably acts through pathways that induce natural sleep and produces electrophysiological changes very similar to those of physiological slow-wave sleep (Bonhomme, Boveroux, & Brichant, 2013). Indeed, according to Alkire (2009), anesthetic interactions with sleep pathways may be characteristic to sedative agents or anesthetics given at sedative doses. However, one must bear in mind that, contrary to the well-defined physiological sleep states, the anesthetic state is behaviorally and electrophysiologically much more heterogeneous (Bonhomme et al., 2013), which makes it challenging both to detect and to compare to physiological sleep.

Anesthesia Awareness

It is relatively common that anesthetized patients report subjective experiences after recovery from anesthesia. However, these experiences are usually reported retrospectively and it is thus difficult to assess whether they have occurred during the actual anesthesia or whether they originated from the recovery period when the effects of the anesthetic drug were dissipating.

Awareness with recall after surgery under general anesthesia is an infrequent but nowadays a well-studied phenomenon. In the clinical practice of anesthesiology, the term anesthesia awareness is used, and it refers both to the actual awareness during surgery (intraoperative awareness) and to the subsequent explicit recall of it (Mashour & LaRock, 2008). Being aware during anesthesia can entail, for example, hearing noises or conversations in the operating room, feeling of being awake or paralyzed, and even pain (Bruchas, Kent, Wilson, & Domino, 2011).

Already the first anesthetists in the 1840s were familiar with the possibility of awareness during surgery (Simini, 2000), but the long-term consequences of this phenomenon from the patient's perspective were not fully recognized until the 1990s, when the number of reports started to increase considerably (Ghoneim, Block, Haffarnan, & Mathews, 2009). It is now known that some of the patients who experience anesthesia awareness may develop subsequent severe psychological symptoms, even a post-traumatic stress disorder (PTSD) (Osterman, Hopper, Heran, Keane, & van der Kolk, 2001).

In recent studies, the incidence of anesthesia awareness has been shown to be approximately 0.10–0.14% (Mashour et al., 2012; Samuelsson et al., 2008a; Sebel et al., 2004) in the Western countries, although a recent comprehensive study in the UK yielded a considerably lower prevalence of 0.005% (Pandit et al., 2014). In China, for example, the prevalence has been reported to be somewhat higher: 0.41% (Xu, Wu, & Yue, 2009). The majority of the anesthesia awareness studies have been conducted in a clinical environment on patients undergoing surgical operations, and thus a number of intervening factors need to be considered, such as the length and depth of the required anesthesia, the condition of the patient, and the combination of anesthetic agents and other medication. All these may affect the presence and recall of subjective experiences during anesthesia (Noreika et al., 2011).

Some patient groups are especially vulnerable to anesthesia awareness and are said to be at high risk for it. These include, for example, cardiac surgery patients (Dowd et al., 1998), women undergoing cesarean section under general anesthesia (Lyons & Macdonald, 1991), trauma patients (Bogetz & Katz, 1984) and people with history of anesthesia awareness (Aranake et al., 2013). Also children seem to be more prone to anesthesia awareness with the reported prevalence of approximately 1% (Davidson et al., 2005; Lopez et al., 2007). However, despite the elevated risk for awareness among pediatric patients, the risk for psychological sequelae seems to be lower in this group (Lopez, Habre, van der Linden, & Iselin-Chavez, 2008; Phelan, Stargatt, & Davidson, 2009).

The question of anesthetic depth arises inevitably in connection with anesthesia awareness, since light anesthesia has been shown to be the most common cause for it (Ghoneim et al., 2009). Bispectral index monitor (BIS) is one of the most widely used monitors in defining the depth of anesthesia, but has not proven to be an effective tool in predicting or preventing intraoperative awareness with explicit recall in unselected surgical population (Mashour et al., 2012), or with high-risk surgical patients (Avidan et al., 2008; Avidan et al., 2011) despite the initial promising results with the high-risk population (Myles, Leslie, McNeil, Forbes, & Chan, 2004). Hence, the neurophysiological measurements and algorithms used to translate these measures into estimates of anesthesia depth are still lacking considerably in their ability to detect anesthesia awareness.

Anesthesia Dreaming

Dreaming offers a unique window to the subjective contents of consciousness. According to Revonsuo (2006) and Mashour (2011), dreaming can be regarded as pure subjectivity, since during dreaming one is generally disconnected from both sensory input and motor output, and conscious experiences are internally generated. In addition to natural sleep, dreaming can also appear in connection with anesthesia, although it remains unclear whether this dreaming takes place during the actual anesthesia or the recovery period, since the anesthetized patients have been able to be interviewed only after the recovery.

Anesthesia dreaming has been defined as a recalled experience, other than awareness, taking place between the induction of anesthesia and the recovery of consciousness upon emergence from anesthesia (Hobbs, Bush & Downham, 1988). There is evidence that anesthesia dreaming was a familiar concept already at the dawn of anesthesia in the 1840s (Bigelow, 1846), but it was not until the 1960s onward that the phenomenon received wider attention among researchers. In the 1960s and 1970s, the frequency estimates of this phenomenon varied a great deal: In 1960, Hutchinson reported dreaming in 3% (Breckenridge & Aitkenhead, 1983), Wilson, Vaughan and Stephen (1975) in 8% and, Brice, Hetherington and Utting (1970) in 44% of patients undergoing general anesthesia.

More recently, it has been reported that approximately one fifth of patients give dream reports when interviewed on emergence from general anesthesia

(Leslie et al., 2007; Brandner et al., 1997). Similar numbers have been reported with sedation (Sing Yi Eer, Padmanabhan, & Leslie, 2009; Stait et al., 2008). However, the incidence of dreaming reported in postanesthesia interviews can still vary greatly even between large-scale studies, e.g. from 6% (Leslie et al., 2005) to 53% (Errando et al., 2008). In the experimental study by Noreika et al. (2011), conducted with healthy young participants anesthetized with single anesthetic agent, the subjects reported a dreaming incidence of 59%.

The patients that report dreams after recovery are usually younger and healthier and have high home dream recall, they usually also receive propofol as the main anesthetic and emerge quickly from the anesthesia (Leslie et al., 2007; Sing Yi Eer et al., 2009). The dream report rate is usually higher (up to 40%) when only propofol is used as an anesthetic (Kasmacher, Petermeyer, & Decker, 1996; Brandner et al., 1997; Kim, Joo, Sung, Kim, & Shin, 2011). This may be due to speedier emergence from anesthesia enabled by propofol, a lesser degree of amnesia specific to it, or an indication that for some reason propofol does not suppress the neural mechanisms of dreaming to the same extent than most other anesthetics do.

The contents of the dreams seem to be fairly similar for both general anesthesia and sedation (Strait et al., 2008). The dreams tend to be short and pleasant in nature and relate to everyday life and, thus, lack the vivid and bizarre qualities characteristic to REM sleep dreams (Leslie & Skrzypek, 2007; Aceto et al., 2007; Kim et al., 2011). Kasmacher et al. (1996) reported already in the 1990s about pleasant dreaming in connection with propofol.

Overall, there has been very little research on the contents of anesthesia dreaming and awareness. Practically, the only comprehensive content analysis was conducted by Noreika et al. (2011), using the Subjective Experiences During Anesthesia Coding System (SEDA-scale) specifically developed for their experimental study with four different anesthetic agents (propofol, dexmedetomidine, sevoflurane and xenon). With SEDA, subjective experiences are divided into three categories: micro-level (including various sensory and affective experiences), macro-level (e.g. dream-like or laboratory-related experiences) and white reports where the participant recalls having had some experiences but not their content. The coding system showed a significant difference between anesthetic agents in the number of laboratory-related experiences: sevoflurane induced more laboratory-related experiences than dexmedetomidine did but the number of these or any other experiences did not differ significantly between dexmedetomidine and propofol (Noreika et al., 2011).

There have been conflicting results concerning the depth of anesthesia and its relation to anesthesia dreaming. This is an important question since one must consider the possibility of dreaming being related to near-miss awareness during anesthesia. The connection between anesthesia dreaming and awareness has been studied and it has been found that, although there is an association between these two phenomena, anesthesia dreaming does not in any case predict anesthesia awareness (Samuelsson et al., 2008a). In many studies, BIS has been used in defining the depth of anesthesia and its predictive powers in relation to dreaming have been both endorsed and questioned. Sing Yi Eer et al. (2009) reported that dreaming during sedation is associated with higher propofol doses and deeper anesthesia (lower BIS values), whereas Noreika et al. (2011) associated subjective experiences with lighter anesthesia (higher BIS values) when dexmedetomidine was used. Leslie et al. (2007), however, concluded that anesthesia dreaming is not related to anesthesia depth in almost any cases and, hence, does not correlate with lower BIS values. Samuelsson, Brudin, and Sandin (2008b) reported similar results against the predictive powers of BIS in their large scale study by concluding anesthesia dreaming to be a separate phenomenon, and generally unrelated to insufficient anesthesia indicated by high BIS levels.

Present Study

It is known that subjects undergoing general anesthesia sometimes report externally induced or internally generated subjective experiences after anesthesia, i.e. anesthesia awareness or dreaming. However, almost all studies on these phenomena have been conducted with surgical anesthesia in a clinical setting, except for Noreika et al. (2011). In all of these studies, including the one by Noreika et al., the subjects have been interviewed only after they have recovered from anesthesia. Hence, it cannot be established with certainty at which point in time the anesthesia-related subjective experiences have taken place. The reports collected upon the spontaneous emergence from anesthesia cannot be interpreted with certainty to represent anesthesia awareness or dreaming as they may be the product of recovery-related physiological sleep. Further, in only one previous study, in the study by Noreika et al., the contents of anesthesia dreaming and awareness have been studied in detail.

This study aims to avoid the shortcomings of previous studies by addressing anesthesia awareness and dreaming in healthy young participants anesthetized with a single anesthetic agent, and who are attempted to be awakened directly from anesthesia and interviewed without a recovery period. Also, to render the results of the present study comparable to the results of the previous studies, and to be able to compare the frequency and content of the reports obtained during infusion to those obtained after a recovery period, the participants were also interviewed after they spontaneously woke up after the anesthetic infusion had been terminated.

In this study, we applied two different anesthetic agents, either propofol or dexmedetomidine, to young and healthy male subjects in a nonsurgical experimental setting. No additional medication or anesthetic agent combinations were used. In addition to interviewing our subjects upon the emergence from anesthesia after a recovery period, we attempted to awaken and interview them once or twice during the actual anesthesia in order to establish whether the subjective experiences take place during the actual anesthesia or the recovery period. By using this approach, we aimed to capture the true nature of anesthesia-related experiences more accurately.

The research questions of the present study were:

1) How often are subjective experiences reported by participants anesthetized with propofol and dexmedetomidine when they are awakened and interviewed during their period of unresponsiveness and upon emergence from anesthesia after a short recovery period? Do blood plasma drug concentration levels or spontaneous arousals during the unresponsiveness period associate with the reports on subjective experiences?

2) What are the specific contents of the reports on subjective experiences during and after anesthesia, and do propofol and dexmedetomidine lead to reporting similar kinds of experiences? How frequently the reports on subjective experiences include anesthesia awareness versus anesthesia dreaming after unresponsiveness induced with propofol and dexmedetomidine?

Methods

This study was performed as a part of the Academy of Finland funded Conscious Mind project, an extensive experimental series exploring brain activity changes that are related to anesthesia and natural sleep using various methodological approaches, such as electroencephalography (EEG), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI). First person reports were used for studying the subjective experiences originating from anesthesia and sleep. The study protocol was approved by the Ethics Committee of the Hospital District of Southwest Finland (Turku, Finland) and the Finnish Medicines Agency (Fimea). The study was registered in ClinicalTrials.gov (NCT01889004, Parts1−2) and a written informed consent was acquired from all the participants.

Participants

The participants were recruited from student and staff mailing lists from the University of Turku, the Åbo Akademi University, and the University of Applied Sciences in Turku. The participants were required to be non-smoking right-handed males at the age of 20−30 years and have a good general health (American Society of Anesthesiologists (ASA) physical status I) and be fluent in Finnish. Altogether, 47 healthy male volunteers (age range 20−30, M = 23.7 years, SD = 2.47 years) participated in this study. All the participants underwent a pre-study interview and laboratory tests, including a hearing test, drug screening and an electrocardiogram (ECG) recording. None of the participants had previously been diagnosed with a psychiatric or neurological disorder, had substance abuse problems, drug allergies or ongoing medications or suffered from a somatic illness of clinical relevance. Additionally, all the participants restrained from using alcohol and medication for 48 hours prior to the study sessions and fasted overnight before the anesthetic induction.

Study Outline

The experiment was conducted in a nonsurgical experimental setting during one session. After the procedure was explained to the participant, and all preparations made, the experiment began by a four-minute recording of the participants' baseline EEG (2 min eyes open and 2 min eyes closed). Then, to measure the N400 event related potential (ERP), a block of 150 congruent and incongruent sentences was presented via headphones and the participant was required to answer them by pressing either of the two response handles attached to his wrists. Also, before starting the drug infusion, a mismatch negativity (MMN) stimulus block was presented to which the participant did not have to respond in any way. The results of these two paradigms are presented elsewhere.

The participants were randomly anesthetized with either of the two anesthetic agents: propofol (*n*=24) or dexmedetomidine (*n*=23). The anesthetic agent was selected randomly with balanced randomization and no additional medication or anesthetic agent combinations were used. The participants were anesthetized with target controlled infusion by stepwise increasing the anesthetic dosage at five minute intervals until they reached a state of unresponsiveness. Their state of responsiveness was tested with standardized sentence stimuli (R-test, a block composed of five congruent and five incongruent sentences) five minutes after the induction or the dosage increase of the anesthetic agent. The R-test was presented via headphones and the participants were to respond to it by pressing the handles according to instructions. In the absence of a response to any of the sentences (0/10), the participant was deemed to have lost his responsiveness (LOR1). During the following approximately 25 minutes of unresponsiveness, N400 and MMN stimulus blocks and an emotionally unpleasant sound stimulus, the so-called incorporation sound, were presented. The incorporation stimulus was presented two minutes before the attempted awakening, with the aim to measure whether the participants would report hearing the sound (which would signify connectedness and anesthesia awareness) or whether it would be incorporated into possible dream content (signifying partial connectedness combined with internally generated subjective experiences). Then, the participant was attempted to be awakened by calling his name combined with the command "open your eyes" and a light shaking of the shoulder. In case the participant responded, he was regarded to have recovered his responsiveness (ROR1). At this point, the participant was interviewed for the first time about his subjective experiences with a semi-structured interview.

After the first interview, the participant was left unstimulated without an increase in the anesthetic dosage in the hope that the participant would become unresponsive again with the same drug dose. Responsiveness was again tested at five minute intervals on altogether four occasions if needed. In case of no response, the second loss of responsiveness (LOR2) was deemed to have taken place, the stimuli were again presented as described above, and eventually the second recovery of responsiveness (ROR2) was attempted as in LOR1. In case of a successful recovery, the second interview was conducted. After the interview, or in case LOR2 or ROR2 were not reached, the anesthetic dosage was increased to 1.5 fold in order to reach a certain loss of consciousness (LOC). Following this unresponsive period, whose protocol was identical to that of LOR1 and LOR2, the final recovery of responsiveness (ROR3) was allowed to occur spontaneously and was monitored by repeating the standardized R-test via the headphones. In case the participant did not react spontaneously within 30 minutes, an awakening was performed in the same manner as previously. The final interview was then conducted immediately after the recovery of responsiveness (see Figure 1 for an overview of the study protocol).

After the final interview, the participants performed an additional forced-choice task that was related to the stimuli presented during the experiment. Then, the participants were allowed to rest until they had fully recovered from the effects of anesthesia. The local standard post-anesthesia discharge criteria were applied to determine when the participants were allowed to leave the study premises with an escort.

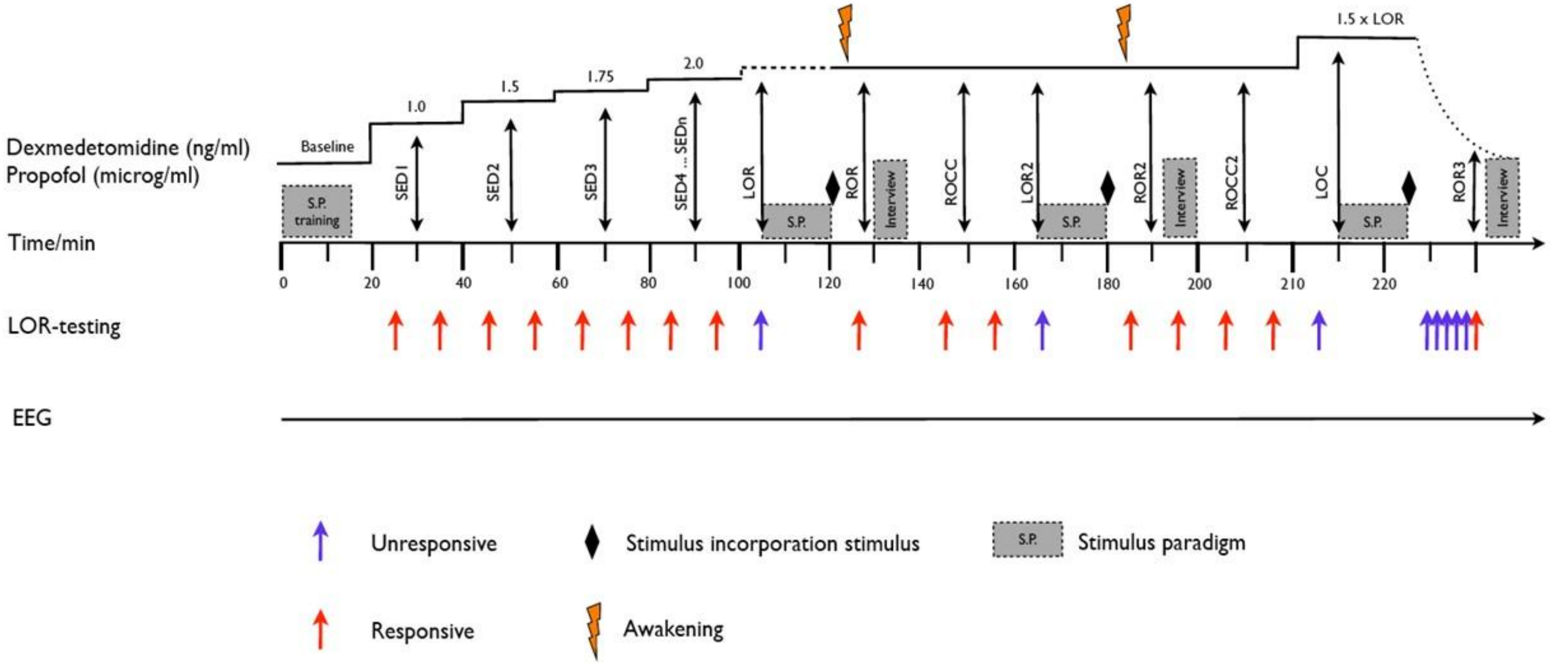

Figure 1. *Study procedure*

SED = sedation; LOR = loss of responsiveness; ROR = recovery of responsiveness; ROCC = recovery of consciousness; LOC = loss of consciousness

Interviews

After every successful awakening (ROR1, ROR2, ROR3), the participants were interviewed on their subjective experiences during anesthesia. The interview was conducted immediately after the participant responded to the awakening procedure. The total number of interviews per participant depended on whether the awakenings from LOR1 or LOR2 were successful or not, but each participant was interviewed at least once, i.e. after the final awakening (ROR3). The aim of the interviews was to find out how frequently the participants had subjective experiences during anesthesia, what kinds of experiences, and whether these experiences were related to the ERP paradigm stimuli or incorporation stimuli, signifying awareness of the environment.

The semi-structured interview of this study was a modified version of Brice’s questionnaire (Brice et al., 1970) (see Table 1 for the structure of the interview). The participants were informed of its contents before the experiment. The questions concerned the subjective experiences the participant had possibly had during the anesthesia and were presented in an open, non-leading manner. In case the participants answered yes to any question, they were asked to describe the experience in as much detail as possible. The participants were first inquired whether or not they had dreamt and, in case they had, about the specific dream contents. Then they were inquired about their possible awareness of environment during anesthesia with a series of questions on their anesthesia-related sensory perceptual experiences. In the final interview, the participants were additionally inquired about the last experience before falling asleep for the first time and the first experience after the final awakening in order to assess the subjective timeline of anesthesia. The interviews were recorded digitally and transcribed word by word for systematic content analysis.

Table 1.

The interview questions. If the participant answered yes to any question, he was asked to describe the experience in as much detail as possible.

1. Did you have a dream during anesthesia?
2. Did you experience anything related to this room during anesthesia?
3. Did you hear anything during anesthesia?
4. Did you sense anything (else) during anesthesia?
5. Do you remember something else from during anesthesia that you have not already mentioned?

Additional questions for the final awakening:

6. What is the last thing you remember before falling asleep for the first time?
7. What is the first thing you remember after awakening?

Content Analysis

The transcripts of the interviews on the participants' subjective experiences during anesthesia were systematically content analyzed. The analysis was performed by two independent judges with a modified SEDA coding tool. In the first phase, the aim was to separate the anesthesia reports from the non-anesthesia reports. Anesthesia reports refer to reports that include subjective experiences that most likely have occurred after anesthesia induction, during LORs or LOC, or during unresponsiveness when recovering from LOC before the last awakening. Non-anesthesia reports refer to those experiences that have taken place before anesthesia induction, during spontaneous arousals or RORs, or after the recovery. A white report, in contrast, refers to occasions where the participants thought they had had experiences during anesthesia, but could not recall any content. The report coding system is summarized in Figure 2 and presented in more detail in Table 2.

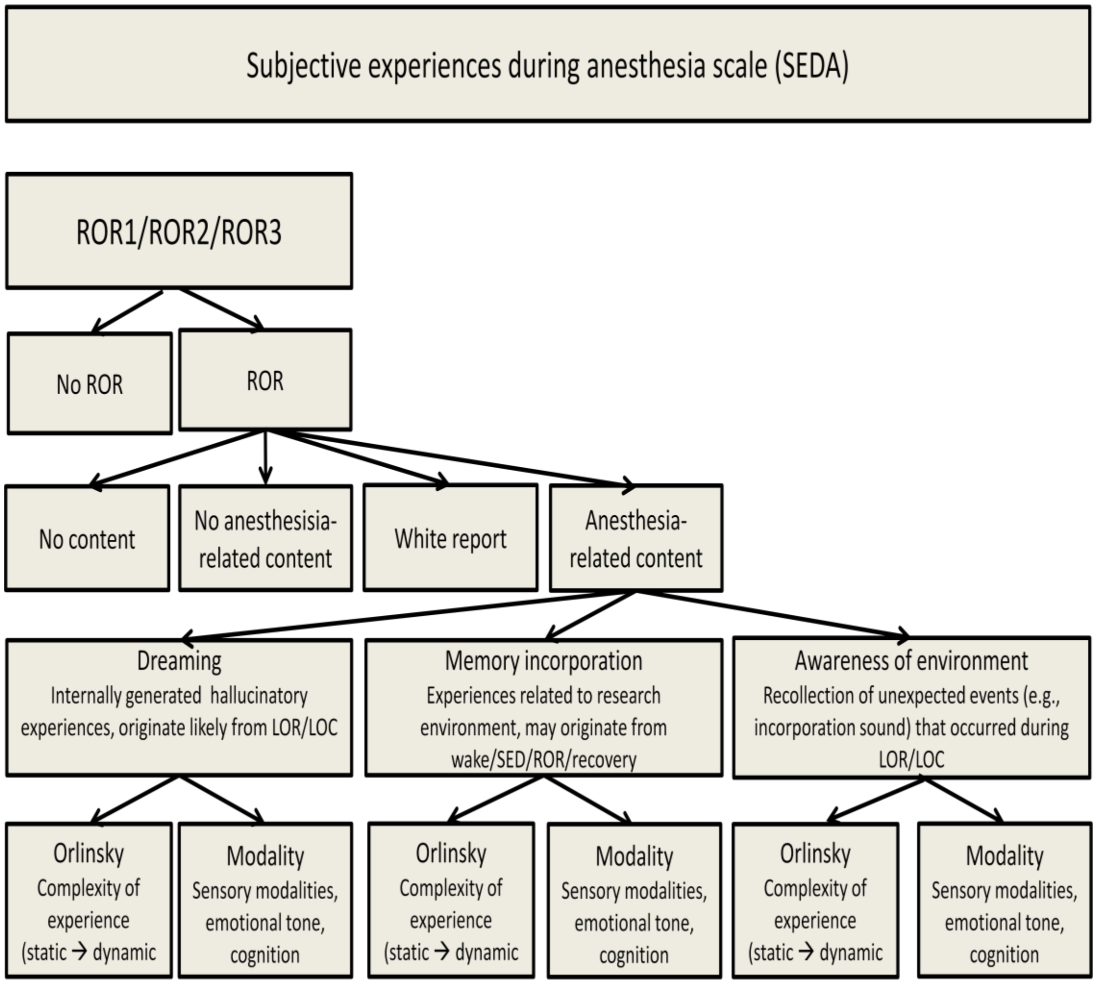

Figure 2. *Overview of the content analysis procedure*

In the second phase, the anesthesia reports were further classified into those that included internally generated subjective content, i.e. dreaming or direct memory incorporation of the research setting or awareness of the environment. The aim was to find out how many of the anesthesia reports included purely internally generated hallucinatory content, how many reflected memory incorporations of the research environment, and how many included pure incorporation of stimuli that was present only during LORs/LOC, such as recollection of the incorporation sound or events the participant could not have expected to occur during the experiment.

In the third stage of analyses, the perceptual complexity of the anesthesia report content was evaluated. This was done by applying the modified version of Orlinsky's (1962) scale. The scale originally includes seven complexity categories, which were compressed into three for the purposes of the present study, ranging from static to more dynamic perceptual experiences. An additional category of 0 was used when the report did not include any perceptual content or included only thought or emotion content and was thus regarded as perceptually void.

In the final stage of the analysis, the perceptual content of the anesthesia reports was classified with 13 categories for modality of sensation or perception, affective states, cognition, out-of-body experiences, and sense of presence. A single report may have included various experiences from different modalities.

Table 2.

Content analysis scale for the classification of the interview reports

All interviews were coded:

No awakening	The subject has not woken up after either LOR1 or LOR2 (ROR has not been achieved).
Awakening but no report	The subject has regained consciousness, but there is no report of any experiences, not even a white report.
Non-anesthesia report (wake reports)	Experiences only before anesthesia induction or after recovery of consciousness. Any sensations or perceptions, thoughts, emotions, etc. reported from before the infusion has been started or after the participant has woken up.
White report	Experiences during anesthesia (after infusion was started but before awakening), the participant remembers something but no explicit content.
Anesthesia report	A report from during anesthesia, i.e. any sensations, perceptions, thoughts, emotions that have been experienced after infusion has been started but before the participant has woken up. Can include experiences from after infusion, but before LOR or from during LOR.

Anesthesia reports were further coded:

Anesthesia dreaming	Internally generated dream-like hallucinatory experiences, i.e., reports content of consciousness that is not directly related to or does not originate from the research environment.
Memory incorporation	Subjective experiences related to things/persons that have been present or events that have occurred during the anesthesia session, but which may be memory incorporation from experiences during wakefulness before the experiment was

	started or from the very beginning of the experiment when the infusion has been started.
Anesthesia awareness	Subjective experiences related to things/persons that have been present or events that have occurred during the anesthesia session, but which the participant cannot have expected to be present or occur during the session.

Anesthesia dreaming, memory incorporation and anesthesia awareness reports were further separately coded with modified Orlinsky's (1962) scale of perceptual complexity

Static	An isolated, fragmentary percept or several unconnected or interconnected percepts are reported, but there is no information about a more general scene in which the percepts are embedded, and there is no movement.
Scene with objects	A scene is defined as one percept encompassing another so that the scene forms a background for other percepts. The scene may also change from one to another, but there is no movement or change within a single scene.
Dynamic	Dynamic change occurs between several interconnected experiences or between interconnected experiences within a scene or between scenes.

Anesthesia dreaming, memory incorporation and anesthesia awareness reports were further separately coded according to modalities:

Sensations and perceptions	Visual, auditory, interoceptive (hunger, thirst), tactile, kinesthetic, temperature, pain, olfactory, and gustatory experiences.
Affective states	Positive and negative moods and emotions.
Cognition	Thoughts, memories, recollections, planning, etc. cognitive activity.
Out-of-body experience	Observing one's body and/or the laboratory environment from an outside position.
Sense of presence	Sensing a presence next to one's body.

After every independently completed analysis, the inter-rater agreement was evaluated. In case of disagreement, the content of the report was discussed until an agreement was reached or the final decision was made by a third judge.

Statistical Methods

Statistical analyses were performed using SAS System version 9.4 for Windows (SAS Institute Inc., Cary, NC), and IBM SPSS version 24 for Windows^{TM} softwares. Data were mostly analyzed using nonparametric methods due to the skewed distributions and the outlying observations. Differences in the number and content of reports between anesthetics, and whether arousals during unresponsiveness or drug concentration levels associated with reporting experiences or certain types of experiences were analyzed with Mann-Whitney U-test (U), Fisher's Exact Test (*FET*), and Kruskall-Wallis test (H). Possible differences between anesthetics in the time to awakening after infusion was terminated were measured with Independent Samples T-test (t), and whether probability of arousals was similar between RORs with repeated measurements logistic regression analyses with generalized estimating equation (GEE) method. The interrater agreement was evaluated with percent agreement and Cohen's Kappa coefficient. Kappa values $<.4$ indicate weak agreement, values .4−.75 fair to good agreement, whereas values $>.75$ indicate strong agreement (Fleiss, 1981). Significance level was set at $p < .05$.

Results

Inter-rater Reliability

The inter-rater reliability between the two independent judges as measured with percent agreement and Cohen's Kappa coefficient was high for all the coding scales. The reliability for the categorization of the report types was 92.8%, $K = 0.887$, $p < .001$, and for the coding of the anesthesia experiences to include dream-like imagery, memory incorporation or awareness of the environment 98.8%, $K = 0.973$, $p < .001$. The modified Orlinsky scale was applied with an overall reliability of 88.5%, $K = 0.758$, $p < .001$, and the modality scale for sensations and perceptions, affective states, cognition, OBEs and sense of presence with 89.0% (Kappa could not be computed due to the binary nature of the data).

Awakenings, Drug Concentrations, Arousals and Report Frequency

Two anesthesia sessions were terminated after LOR1 due to the participants' apnea. No data was obtained from one participant, and from the other, data from only ROR1 was eligible. Thus, the final number of participants was 46, of which 23 received propofol and 23 dexmedetomidine, but only 45 participants reached the LOC state. The number of successful awakenings during steady infusion (ROR1, ROR2) was significantly higher with participants receiving dexmedetomidine than propofol ($p < .05$ for ROR1, $p < .05$ for ROR2, *FET*) (see Table 3 for details). Additionally, significantly fewer of the propofol participants that were arousable from LOR1 were able to re-enter the state of unresponsiveness, i.e. to reach LOR2 ($p < .001$, *FET*).

Table 3.

Frequency of awakenings during anesthesia

	ROR1 n (%)	ROR2 n (%)	ROR3 n (%)
Both drugs	28/46 (60.1%)	20/22~ (90.1%)	45/45~~ (100.0%)
Dexmedetomidine	18/23 (78.3%)*	18/18 (100.0%)*	23/23 (100.0%)
Propofol	10/23 (43.5%)*	2/4 (50.0%)*	22/22 (100.0%)

~LOR2 was attempted with those 28 participants who achieved ROR1, but six propofol participants did not re-enter unresponsiveness. Thus, only 22 LOR2s were attempted.
~~ With one subject the experiment was discontinued after LOR1 due to apnea.
* Statistically significant difference between drugs, $p < .05$ (Fisher's Exact Test).

The target concentration for LOR varied individually between between 1.0 and 3.25 ng/ml for dexmedetomidine and 1.0 and 2.75 μg/ml for propofol. The mean (SD) measured concentration for LOR was 2.06 (0.66) ng/ml for dexmedetomidine and 1.67 (0.62) μg/ml for propofol, and for LOC 3.13 (0.94) ng/ml and 2.63 (0.79) μg/ml, respectively. The measured LOR or LOC concentration was not associated with achieving ROR1 or ROR2 with either of the anesthetics (all *p*s > .05, *U*-test), or reporting anesthesia experiences (all *p*s = .05, *H*-test).

There was no significant difference between the drugs in the time it took for the participants to emerge from anesthesia (ROR3) after the anesthetic infusion had been terminated ($t(43) = .74$, $p = .47$), although it varied greatly between the participants with both drugs (M_{dex} = 1212 s, SD_{dex} = 745 s; M_{prop} = 1059 s, SD_{prop} = 641 s). Further, the time to awakening did not correlate with the drug concentration level measured in the LOC state with either anesthetic and did not associate with the number or type of reports given after the awakening (all *p*s > .05).

There were no differences between the drugs in the number of arousals during the anesthetic infusion ($p = .05$). However, when comparing whether there was an arousal during the preceding state (LOR/LOC) within drugs, with dexmedetomidine participants a significant difference with repeated measurements logistic regression analysis was found between the stages ROR1 vs. ROR2 (13.0% vs. 38.9%, $p < .05$) and ROR2 vs. ROR3 (38.9% vs. 13.0%, $p < .05$) in that there were more arousals in ROR2. Having an arousal during the preceding unresponsive period (LOR1 or LOR2) did not associate achieving ROR or with reporting anesthesia experiences (all *p*s >.05).

Anesthesia Experiences

With both drugs, the majority of successful awakenings led to a report including anesthesia experiences, and in ROR3, the participants receiving dexmedetomidine reported significantly more often anesthesia experiences than the propofol participants (95.7% vs. 72.7%, $p < .05$, *FET*) (see Table 4 for further details).

Table 4.

Frequency of anesthesia reports

	ROR1 n (%)	ROR2 n (%)	ROR3 n (%)
Both drugs	25/28 (89.3%)	15/20 (75.0%)	38/45 (84.4%)
Dexmedetomidine	17/18 (94.4%)	14/18 (77.8%)	22/23 (95.7%)*
Propofol	8/10 (80.0%)	1/2 (50.0%)	16/22 (72.7%)*

* Statistically significant difference between drugs, $p < .05$.

When the participants reported anesthesia experiences, dreaming (i.e. internally generated hallucinatory subjective experiences not related to the study environment) was the most frequently reported content with both anesthetic agents (Table 5). However, there was a significant difference between the drugs in ROR1: participants anesthetized with dexmedetomidine reported more dreaming than those receiving propofol (100% vs. 62.5%, $p < .05$, *FET*). Additionally, the drug concentration level of dexmedetomidine was associated with whether or not the report contained dreaming both in ROR2 ($p < .05$, *H*-test) and in ROR3 ($p < .05$, *H*-test), so that higher concentrations related to reporting dream-like content (ROR2: $M = 2.10$ ng/ml vs. 1.12 ng/ml; ROR3: $M = 3.33$ ng/ml vs. 1.84 ng/ml).

Table 5.

Type of anesthesia experiences

	ROR1 n (%)	ROR2 n (%)	ROR3 n (%)
Dream-like experiences	22/25 (88.0%)	12/15 (80.0%)	33/38 (86.8%)
Dexmedetomidine	17/17 (100%)*	12/14 (85.7%)	20/22 (90.9%)
Propofol	5/8 (62.5%)*	0/1 (0.0%)	13/16 (81.3%)
Memory incorporation	22/25 (88.0%)	8/15 (53.3%)	30/38 (78.9%)
Dexmedetomidine	15/17 (88.2%)	7/14 (50.0%)	16/22 (72.7%)
Propofol	7/8 (87.5%)	1/1 (100.0%)	14/16 (87.5%)
Awareness	4/25 (16.0%)	4/15 (26.7%)	5/38 (13.2%)
Dexmedetomidine	4/17 (23.5%)	4/14 (28.6%)	4/22 (18.2%)
Propofol	0/8 (0.0%)	0/1 (0.0%)	1/16 (6.25%)

* Statistically significant difference between drugs, $p < .05$.

Direct memory incorporations of the experimental setting were also commonly reported with both drugs (Table 5). In contrast, the reports containing awareness of the environment, i.e. incorporation of events from the study environment that the participant could not have known or expected to occur during LOR or LOC, was infrequent and, when checked against EEG-recordings, always related to brief arousals during the unresponsive state. None of the participants reported a direct reference to the incorporation sound. With all RORs combined, awareness of the environment was more common in those receiving dexmedetomidine than those receiving propofol ($p < .05$, *FET*). Drug concentration levels were not associated with reporting either memory incorporation or awareness of the environment (all *p*s for both drugs > .05).

Perceptual Complexity of Anesthesia Experiences

Perceptual complexity was coded separately for dream-like experiences, for memory incorporations, and for experiences referring to awareness of the environment using the modified Orlinsky scale (1962). The majority of the dream-like experiences contained perceptual content (95.5%). The complexity of the dream-like content was quite equally distributed: static content was reported most often (35.8%), content containing scenes second (34.1%), and the most complex, dynamic content was reported the least (25.5%). There were no significant differences between the awakenings or the anesthetic agents in the complexity of the dream-like content (all ps $< .05$).

The majority of the reports containing direct memory incorporations also included perceptual content (94.7%). Most often the perceptual content in memory incorporation reports was static (80.9%) in nature. Additionally, a few reports contained scenes (13.9%), whereas none of the memory incorporation reports included any dynamic content. There were no significant differences between the awakenings or the anesthetic agents in the complexity of the perceptual content in the memory incorporation reports (all ps $> .05$).

There were altogether 13 reports that contained references to awareness of the environment (ROR1 = 4; ROR2 = 4; ROR3 = 5), and only one of them was reported by a participant receiving propofol, in a ROR3 awakening. All but one awareness experience included perceptual content, and the majority of the content was static in nature (11/13). None of the reports included any scene content and only one included dynamic content.

Sensory-Perceptual, Emotional and Cognitive Content of Anesthesia Experiences

The coding tool for investigating the nature of sensory-perceptual, emotional and cognitive content was used separately for dream-like experiences, for memory incorporations, and for experiences referring to awareness of the environment. The majority of the dream-like content in the reports was visual in nature (89.1%). There were also some auditory experiences (31.1%), thoughts and memories (30.0%), and experiences related to kinesthesia and balance (27.8%). The subjects reported also some positive emotions (20.0%) and negative emotions (12.3%), whereas interoceptive, touch, pain and temperature, gustatory and presence experiences were extremely rare (< 3.0%).There were neither out-of-the-body nor olfactory experiences reported in the dream material.

The coding modalities were grouped into 3 sum variables of sensations (visual, auditory, olfactory, gustatory, interoception, touch, pain and temperature, kinesthesia and balance), emotions (positive and negative emotions) and cognition (thoughts and memories), and further analyzed. In the analysis of the dream reports, there were no significant differences between the drugs in the number of sensations, emotions or cognitions in ROR1 or ROR3 (there were no such content with propofol in ROR2). In ROR1 and ROR2, the majority of the dream reports (19/22 and 9/12, respectively) contained one to two sensations, while emotions (8/22 and 2/12) and cognitions (5/22 and 3/12) were less frequent. In ROR3, the frequencies were fairly similar: majority of the reports contained one to two sensations (28/33), although there were also two reports that contained four to five sensations. Emotions were infrequently reported in the ROR3 dream reports (12/33), whereas there were somewhat more cognitions present (14/33) in this stage as compared to the previous ones.

The majority of the direct memory incorporations included auditory experiences (66.6%), whereas a third contained visual experiences (33.0%). Some of the reports also included experiences related to kinesthesia and balance (26.6%), pain and temperature (17.6%), touch (15.4%), and thoughts and memories (14.7%). In fact, there was a significant difference between the anesthetic agents in ROR1, where there were more reports containing pain and temperature experiences with propofol (3 vs. 0, $p < .05$, *FET*), as well as in ROR3, where the propofol participants reported more thoughts and memories than the dexmedetomidine participants (4 vs. 0, $p < .05$, *FET*), although the number of these experiences was very small. Interoceptive experiences, positive and negative emotions, and sense of presence were rare (< 10.5 %) and gustatory, olfactory or out-of-the-body experiences were not mentioned in the reports containing memory incorporations.

The 13 reports containing references to awareness of the environment included mostly auditory experiences (8/13). There were also some references to the felt presence of someone nearby in one report in all of the awakenings (ROR1 = 1/4; ROR2 = 1/4; ROR3 = 1/5). There were no positive emotions, interoceptive, olfactory, gustatory or out-of-the-body experiences included in the reports referring to the awareness of the environment.

Examples of the classifications of anesthesia experiences are described in Table 6.

Table 6.

Examples of anesthesia experiences

Drug	Type of anesthesia report	Orlinsky	Sensation, perception, emotions, OBEs, sense of presence	Summary of verbal report
Dexmed	Dream	Scene	Visual, kinesthesia/balance, positive emotion	A hunting dream, which was set in a forest, and there were friends present, with whom he communicated “by waving or something”. He “walked there in the forest”, and the atmosphere was “quite relaxed and good”.
Propofol	Dream	Dynamic	Visual, auditory, positive emotion, thoughts/memories	He was studying music in the hospital, and was running late for the experiment. His sister and “some strangers” talked, and the atmosphere was “unreasonably calm considering I had forgotten to come here.”
Dexmed	Memory incorporation	Scene	Visual, auditory, pain/temperature, kinesthesia/balance	Reported being in a similar kind of medical experiment, where he was “lying right here” and a “same kind of person” was administering the drug as in the present experiment. He also remembered talking during the experiment and sensing how “the drug got into his vein”.
Propofol	Memory incorporation	Static	Auditory, pain/temperature	Heard ”people talk”, and recalled the announcement on the anesthesia induction and how the anesthetic

				stung in his arm.
Dexmed	Awareness	Static	Auditory, kinesthesia/balance	Reported having heard sentence stimuli during anesthesia: ”I think I woke up in the middle of [anesthesia].” Recalled also having answered to the stimuli by pressing the handles, which was also confirmed by the researchers.
Propofol	Awareness	Static	Touch, kinesthesia/balance, presence	Reported upon emergence from anesthesia that ”I had apparently moved my arm, and someone came and moved it back to its place.” This had happened “long ago”. The researchers had moved the arm as it fell of the side of the bed.

Discussion

In the present study, the subjective experiences during dexmedetomidine and propofol induced unresponsiveness were explored. As comparison to previous studies, a novel methodological approach was applied, i.e. awakenings during steady-state infusion, in order to capture the nature of these subjective experiences more accurately. At the beginning of this chapter, I will briefly summarize the main findings of the study, and discuss their significance. Then I shall discuss the strengths and weaknesses of the study, and lastly, provide the final conclusions.

General Discussion

The results of this experimental single-drug study lend further support for the previous findings on the presence of subjective experiences during anesthesia despite the state of unresponsiveness, i.e. the lack of outer behavioral signs of consciousness. More importantly, the present study is the first where reports were obtained from participants awakened during steady-state anesthesia period, and shows that the subjective experiences do take place during the actual anesthesia infusion instead of only originating from the recovery period. The reports from during the anesthesia and upon the emergence from anesthesia also reveal the varied nature of these subjective experiences both with regard to their perceptual quality and complexity.

Despite the high overall frequency of successful awakenings during the anesthesia, the two anesthetic agents differed in the number of these awakenings: participants anesthetized with dexmedetomidine were significantly more often arousable from steady-state infusion than those anesthetized with propofol. The propofol participants were also significantly less prone to re-enter the state of unresponsiveness if they were successfully awakened during anesthesia. This means that the majority of the anesthesia reports originating from steady-state awakenings were obtained from participants anesthetized with dexmedetomidine (31 vs. 9). This is especially noteworthy with the second awakening (ROR2) where reports were gained from only 2 participants receiving propofol. The frequency of the anesthesia reports also varied significantly between the drugs upon emergence from anesthesia (ROR3), where dexmedetomidine participants related anesthesia experiences more often than the propofol participants, which further complicates the comparison of the anesthesia experiences specific to the two anesthetics in question.

Notably, the measured blood plasma concentration levels were not associated with achieving ROR1 or ROR2 with either of the anesthetics, or reporting anesthesia experiences. Further, an arousal during the unresponsive period did not increase the likelihood of reporting anesthesia experiences. The fact that in ROR3 time to awakening was not associated with reporting experiences or specifically anesthesia experiences indicates that experiences do not become more likely or more complex, compared to awakenings during steady infusion, during the recovery period when the effects of the anesthetics are dissipating.

When compared to previous studies, in all but one (Noreika et al., 2011) the data were collected in a clinical setting in conjunction with surgical procedures and multiple drug administrations, and the interviews were conducted after spontaneous recovery. Thus, the most likely explanation for the high frequency of reports in the present study is the experimental setting that allowed the use of a single drug on healthy volunteers and enabled awakenings during steady infusion with closely timed interviews. Notably, when ROR3 awakening results are compared to results obtained by Noreika et al. (2011) in a similar experimental setting, anesthesia experiences were more frequently reported after a brief recovery period in the present study, especially for propofol (dexmedetomidine 95.7% vs. 73.7%, propofol 69.6% vs. 36.8%).

The incidence of dreaming in anesthesia reports was higher in this study than in many previous ones, ranging from 80% to 88% depending on the timing of the awakening. The majority of studies on anesthesia dreaming report that approximately one fifth of the subjects experience dreaming during anesthesia (Leslie et al., 2007; Brandner et al., 1997), although some studies have yielded higher frequencies, ranging from 44% to 59% (Brice et al., 1970; Errando et al., 2008; Noreika et al., 2011). Further, this study was conducted with two anesthetics that have been shown to produce more dream reports than other agents, which may also partly explain the high frequency. Propofol-based anesthesia has been associated with a higher incidence of dreaming in several studies (Leslie & Skrzypek, 2007), and in the study by Noreika et al. (2011), dexmedetomidine was associated with significantly higher dream incidence than propofol. This finding is in line with our study in that the subjects anesthetized with dexmedetomidine reported dream-like imagery significantly more than those anesthetized with propofol in ROR1. This further indicates that the frequency of the subjective experiences (or at least the recall of them) seems to depend on the anesthetic agent in question and highlights the necessity to investigate the effects of anesthetic drugs separately.

The anesthesia reports obtained from the participants in this study included perceptual content in the majority of the cases in all the awakenings (86%−100%). Although the complexity of the dream-like content was equally distributed between static, static including scenery, and dynamic, dynamic imagery was present only in 18.2% (ROR1) to 33.3% (ROR3) of dream-like experiences, which seems to support Leslie and Skrzypek's (2007) statement that most anesthesia dreams are simple in nature.

In relation to natural sleep, Revonsuo (2006) has divided the phenomenal forms of consciousness during sleep into two categories: dreaming and sleep mentation. Dreaming is, according to his definition, complex, organized, temporally progressing and multimodal in nature, whereas sleep mentation is less complex and organized and more like static images or isolated thoughts. According to these definitions, the subjective experiences during anesthesia reported in this study can be regarded more as sleep mentation than dreaming, since they were mainly neither very complex, temporally progressing nor highly multimodal in nature. Typically, the reports with dream-like imagery included only one or two sensory modalities, but were not temporally progressing or complex.

Reports referring to awareness of the environment during anesthesia were rare in our study and always linked to brief arousals that were verifiable from EEG tracings. This supports the findings of other studies indicating the highly infrequent nature of awareness during anesthesia (e.g. Mashour et al., 2012; Samuelsson et al., 2008a; Sebel et al., 2004).

To summarize, internally generated subjective experiences seem to be very frequent under anesthetically induced unresponsiveness, but subjective experiences linked to external stimuli or events are rare. Thus, while consciousness, i.e. the ability to have subjective experiences, seems to be preserved under unresponsiveness, connectedness to the environment disappears already with relatively light doses of anesthetics.

Strengths and Limitations of the Study

This study had many methodological strengths compared to previous studies on the same topic. All the previous studies on anesthesia dreaming and awareness have relied on subjective reports given upon, or sometimes hours after, spontaneous emergence from anesthesia. The reports collected after spontaneous recovery period cannot be verified to represent experiences from during anesthesia as the experiences can also originate from the recovery period when the drug dissipates from the body. In this study, the participants were for the first time awakened and interviewed also during the anesthetic infusion. Hence, this study may offer a more accurate perspective on the subjective experiences during general anesthesia. Additionally, the existence of intervening factors was minimized by conducting the study in a purely experimental setting with young and healthy volunteers who were anesthetized with light doses of one anesthetic with no additional medication used. This setting and procedure may have got us closer to capturing the authentic effect of anesthesia on contents of consciousness as compared to many other studies conducted with surgical patients in a clinical setting.

Surprisingly, the reports obtained from awakenings during steady infusion as opposed to those acquired after spontaneous awakenings were highly similar in frequency and content. This signifies that subjective experiences are possible under the influence of anesthetics, and not related only to recovery period.

The content coding procedure that has been lacking in most other studies on anesthesia dreaming was extensive and detailed, beginning at a more general report level and ending with individual sensory perceptual experiences. We attempted systematically to define the timeline of the subjective experiences and separate the ones specifically related to the anesthesia period, and then conducted a detailed analysis on these anesthesia reports. Only Noreika et al. (2011) have performed a similar content analysis on anesthesia reports with their SEDA coding scale. In addition to classifying the perceptual modalities (as in the original SEDA), we also evaluated the contentual complexity of the subjective experiences with a modified version of the Orlinsky's perceptual complexity scale (Orlinsky, 1962). Hence, we could obtain new and more accurate information on the exact nature of subjective experiences during anesthesia.

One of the limitations of this study was a relatively small sample size. Due to the relatively few successful awakenings of propofol participants from LOR1, and because most of those who were arousable did not re-enter unresponsiveness with the same dose, it was difficult to obtain a comprehensive view of the content of propofol anesthesia reports and compare them to the reports obtained from dexmedetomidine anesthesia. This was the case with the modified Orlinsky (1962) scale: the number of reports in each group was so small that it was not possible to compare the contentual complexity between the anesthetics or the awakening stages. The number of sensations and perceptions was also relatively small, which hindered a more extensive comparison between the drugs and awakenings.

Sampling bias and demand characteristics may also have affected our study. Younger and healthier participants have been shown to have a higher anesthesia dream report frequency (Leslie & Skrzypek, 2007). One possibility is also that our participants had more positive attitude towards dreams, which has been shown to affect dream recall frequency with natural sleep (e.g. Beaulieu-Prevost & Zadra, 2007). We did not, unfortunately, measure attitudes towards dreams. In addition, the instructions on the interview and reporting given to the participants in the beginning of the experiment may have increased the participants' willingness to report more dreaming as they thought that was required of them. The experimental procedure may have also had some effect on the participants' dreaming. Gyulaházi et al. (2015) recently investigated the effect of preoperative imagination on the quality of postoperative dream recall and, in their study, the imagery that was evoked with suggestion just prior to the anesthesia induction was present in 73.2% of the reported anesthesia dream content. This also leaves room for speculation of the role of the N400 sentence stimuli presented prior to and during LORs and LOC on the participants' dream content. However, this analysis is beyond the scope of this thesis.

An additional limitation was that when awakened during anesthesia some of the participants were quite disoriented (especially the participants receiving propofol), or extremely tired (especially those receiving dexmedetomidine), and obtaining a clear answer to the interview questions was sometimes challenging. One question that also remains open is how the anesthesia experiences reported in this study apply in real-life operating theater where the depth of anesthesia is greater and more intervening factors are present.

Another limitation was the difficulty in establishing a clear distinction between the subjective experiences originating from the anesthesia induction period and from the period of actual unresponsiveness. Although some participants became immediately unresponsive with the lowest dose, most participants required several steps of sedation before becoming unresponsive, and thus it is impossible to determine whether experiences reported at ROR1 originate from the sedation period or from the period of actual unresponsiveness. Nevertheless, given the amnestic effects of anesthetics (e.g. Nordström & Sandin, 1996; Ebert et al., 2000), and the length of the unresponsive period (appr. 25 min), it seems unlikely that the participants would report hallucinatory experiences from the sedation period. In contrast, memory incorporations sometimes seemed to link to the induction of anesthesia, such as feeling a coldness in the arm. Nevertheless, reports obtained from ROR2 most certainly reflect experiences from the preceding unresponsive period.

Conclusions

This study supports the previous findings of studies on dreaming and awareness during anesthesia by showing that the presence or absence of conscious experiences during anesthesia cannot necessarily be deduced from behavioral signs.

Although rendered unresponsive with light doses of two different anesthetic agents, dexmedetomidine and propofol, the participants reported subjective experiences when awakened during and after anesthetic infusion in an experimental setting. Dream-like imagery was the most commonly reported subjective experience, but also memory incorporations of the experimental setting were frequent in the reports. In contrast, direct awareness of the environment was rare and linked to brief arousals. The similar frequency and content of reports obtained during the anesthetic infusion as compared to those obtained after the infusion was terminated indicate that the subjective experiences do not only originate from the recovery period following the ending of the drug infusion. Hence, despite rendering the individual unresponsive and disconnected, light experimental anesthesia does not necessarily induce unconsciousness, i.e. absence of subjective experiences.

References

Aceto, P., Congedo, E., Lai, C., Valente A., Gualtieri, E., & De Cosmo, G. (2007). Dreams recall and auditory evoked potentials during propofol anaesthesia. *Neuroreport, 18*, 823−826.

Alkire, M. T. (2009). General anaesthesia and consciousness. In S. Laureys, & G. Tononi (Eds.), *The neurology of consciousness: Cognitive neuroscience and neuropathology* (pp. 118−134). London: Academic Press.

Aranake, A., Gradwohl, S., Ben-Abdallah, A., Lin, N., Shanks, A., Helsten, D. L., Glick, D. B., Jacobsohn, E., Villafranca, A. J., Evers, A. S., Avidan, M. S., & Mashour, G. A. (2013). Increased risk of intraoperative awareness in patients with a history of awareness. *Anesthesiology, 119*, 1275−1283.

Avidan, M. S., Jacobsohn, E., Glick, D., Burnside, B. A., Zhang, L., Villafranca, A., Karl, L., Kamal, S., Torres, B., O'Conner, M., Evers, A. S., Gradwohl, S., Lin, N., Palanca, B. J., & Mashour, G. A.; BAG-RECALL research group (2011). Prevention of intraoperative awareness in a high-risk surgical population. *New England Journal of Medicine, 365*, 591−600.

Avidan, M. S., Zhang, L., Burnside, B. A., Finkel, K. J., Searleman, A. C., Selvidge, J. A., Saager, L., Turner, M. S., Rao, S., Bottros, M., Hantler, C., Jacobsohn, E., & Evers, A. S. (2008). Anesthesia awareness and the bispectral index. *New England Journal of Medicine, 358*, 1097−1108.

Beaulieu-Prevost, D., & Zadra, A. (2007). Absorption, psychological boundaries and attitude towards dreams as correlates of dream recall: Two decades of research seen through a meta-analysis. *Journal of Sleep Research, 16*, 51−59.

Block, N. (1995). On a confusion about a function of consciousness. *Behavioral and Brain Sciences, 18*, 227−287.

Breckenridge, J. L., & Aitkenhead, A. R. (1983). Awareness during surgery: A review. *Annals of the Royal College of Surgeon of England, 65*, 93−96.

Bigelow, H. (1846). Insensibility during surgical operations produced by inhalation. *Boston Medical and Surgical Journal*, *35*, 309−17.

Bogetz, M., & Katz, J. (1984). Recall of surgery for major trauma. *Anesthesiology, 61*, 6−9.

Boly, M., Moran, R., Murphy, M., Boveroux, P., Bruno, M. A., Noirhomme, Q., Ledoux, D., Bonhomme, V., Brichant, J. F., Tononi, G., Laureys, S., & Friston, K. (2012). Connectivity changes *underlying* spectral EEG changes during propofol-induced loss of consciousness. *Journal of Neuroscience, 32*, 7082−7090.

Bonhomme, V., Boveroux, P., & Brichant, J. F. (2013). Anesthesia. In A. E. Cavanna, A. Nani, H. Blumenfeld,, & S. Laureys (Eds.), *Neuroimaging of consciousness* (pp. 183−203). Heidelberg: Springer.

Brandner, B., Blagrove, M., McCallum G., & Bromley, L. M. (1997). Dreams, images and emotions associated with propofol anaesthesia. *Anaesthesia, 52*, 750−755.

Brice, D. D., Hetherington, R. R., & Utting, J. E. (1970). A simple study of awareness and dreaming during anaesthesia. *British Journal of Anaesthesia, 40*, 535−542.

Bruchas, R. R., Kent, C. D., Wilson, H. D., & Domino, K. B. (2011). Anesthesia awareness: Narrative review of psychological sequelae, treatment, and incidence. *Journal of Clinical Psychology in Medical Settings*, *18*, 257−267.

Damasio, A., & Meyer, K. (2009). Consciousness: An overview of the phenomenon and its possible neural basis. In S. Laureys, & G. Tononi (Eds.), *The neurology of consciousness: Cognitive neuroscience and neuropathology* (pp. 3−14). London: Academic Press.

Davidson, A., Huang, G., Czarnecki, C., Gibson, M., Stewart, S., Jamsen, K., & Stargatt, R. (2005). Awareness during anesthesia in children: a prospective cohort study. *Anesthesia & Analgesia*, *100*, 653−661.

Dowd, M., Cheng, D., Karski, J., Wong, D., Munro, J., & Sandler, A. (1998). Intraoperative awareness in fast-track cardiac anaesthesia. *Anesthesiology, 89*, 1068−1073.

Eaton, M. M., Germann, A. L., Arora, R., Cao, L. Q., Gao, X., Shin, D. J., Wu, A., Chiara, D. C., Cohen, J. B., Steinbach, J. H., Evers, A. S., & Akk, G. (2016). Multiple non-equivalent interfaces mediate direct activation of $GABA_A$ receptors by propofol. *Current Neuropharmacology, 14*, 772–780.

Ebert, T. J., Hall, J. E., Barney, J. A., Uhrich, T. D., & Colinco, M. D. (2000). The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology, 93*, 382−394.

Errando, C. L., Sigl, J. C., Robles, M., Calabuig, E., García, J., Arocas, F., Higueras, R., del Rosario, E., López, D., Peiró. C. M., Soriano, J. L., Chaves, S., Gil, F., & García-Aguado, R. (2008). Awareness with recall during general anaesthesia: A prospective observational evaluation of 4001 patients. *British Journal of Anaesthesia, 101*, 178−185.

Fleiss, J. L. (1981). *Statistical methods for rates and proportions* (2nd ed.). New York: Wiley.

Ghoneim, M. M., Block, R. I., Haffarnan, M., & Mathews M. J. (2009). Awareness during anesthesia: risk factors, causes and sequelae: A review of reported cases in literature. *Anesthesia & Analgesia, 108*, 527−535.

Gyulaházi, J., Redl, P., Karányi, Z., Varga, K., & Fülesdi, B. (2015). Dreaming under anesthesia: is it a real possibility? Investigation of the effect of preoperative imagination on the quality of postoperative dream recalls. *BMC Anesthesiology, 16*, 53.

Hobbs, A. J., Bush, G. H., & Downham, D. Y. (1988). Peri-operative dreaming and awareness in children. *Anaesthesia, 43*, 560−562.

Hutchinson, R. (1961). Awareness during surgery: A study of its incidence. *British Journal of Anaesthesia, 33*, 463−469.

Kim, D-K., Joo, Y., Sung, T-Y., Kim, S-Y., & Shin, H-Y. (2011). Dreaming in sedation during spinal anesthesia: A comparison of propofol and midazolam infusion. *Anesthesia & Analgesia, 112*, 1076−1081.

Kasmacher H., Petermeyer, M., & Decker C. (1996). Incidence and quality of dreaming during anaesthesia with propofol in comparison with enflurane. *Anaesthetist, 45*, 146−153.

Leslie, K., Myles, P. S., Forbes, A., Chan, M. T., Swallow S. K., & Short, T. G. (2005). Dreaming during anaesthesia in patients at high risk of awareness. *Anaesthesia, 60*, 239−244.

Leslie, K., & Skrzypek, H. (2007). Dreaming during anaesthesia in adult patients. *Best Practice & Research Clinical Anaesthesiology, 21*, 403−414.

Leslie, K., Skrzypek, H., Paech, M. J., Kurowski, I., & Whybrow, T. (2007). Dreaming during anesthesia and anesthetic depth in elective surgery patients: A prospective cohort study. *Anesthesiology, 106*, 33−42.

Leslie, K., Sleigh, J., Paech, M., Voss, L., Lim, C., & Sleigh, C. (2009). Dreaming and electroencephalographic changes during anesthesia maintained with propofol or desflurane. *Anesthesiology, 111*, 547−555.

Liu, X., Lauer, K. K., Ward, B. D., Rao, S. M., Li, S. J., & Hudetz, A. G. (2011). Propofol disrupts functional interactions between sensory and high-order processing of auditory verbal memory. *Human Brain Mapping, 33*, 2487−2498.

Lopez, U., Habre, W., Laurencon, M., Haller, G., van der Linden, M., & Iselin-Chavez, I. (2007). Intraoperative awareness in children: The value of a questionnaire adapted to their cognitive abilities. *Anaesthesia, 62*, 778−789.

Lopez, U., Habre, W., van der Linden, M., & Iselin-Chavez, I. (2008). Intraoperative awareness in children and post-traumatic stress disorder. *Anaesthesia, 63*, 474−481.

Lyons, G., & Macdonald, R. (1991). Awareness during caesarean section. *Anaesthesia, 46*, 62−64.

Mashour, G. A. (2011). Dreaming during anesthesia and sedation. *Anesthesia & Analgesia, 112*, 1008−1010.

Mashour, G. A., & LaRock, E. (2008). Inverse zombies, anesthesia awareness, and the hard problem of unconsciousness. *Consciousness and Cognition, 17*, 1163−1168.

Mashour, G. A., Shanks, A., Tremper, K. K., Kheterpal, S., Turner, C. R., Ramachandran, S. K., Picton, P., Schueller C., Morris, M., Vandervest, J. C., Lin, N., & Avidan, M. S. (2012). Prevention of intraoperative awareness with explicit recall in an unselected surgical population: A randomized comparative effectiveness trial. *Anesthesiology, 117*, 717−725.

Mhuircheartaigh, R. N., Rosenorn-Lanng, D., Wise, R., Jbabdi, S., Rogers, R., & Tracey, I. (2010). Cortical and subcortical connectivity changes during decreasing levels of consciousness in humans: a functional magnetic resonance imaging study using propofol. *Journal of Neuroscience*, *30*, 9095−9102.

Myles, P. S., Leslie, K., McNeil, J., Forbes, A., & Chan, M. T. (2004). Bispectral index monitoring to prevent awareness during anaesthesia: The B-Aware randomized controlled trial. *The Lancet, 363*, 1757−1763.

Nordström, O., & Sandin, R. (1996). Recall during intermittent propofol anaesthesia. *British Journal of Anaesthesia, 76*, 699−701.

Noreika, V., Jylhänkangas, L., Móró, L., Valli, K., Kaskinoro, K., Aantaa, R., Scheinin, H., & Revonsuo, A. (2011). Consciousness lost and found: Subjective experiences in an unresponsive state. *Brain and Cognition, 77*, 327−334.

Orlinsky, D. E. (1962). Psychodynamic and cognitive correlates of dream recall. Unpublished doctoral dissertation. Chicago: The University of Chicago.

Osterman, J. E., Hopper, J., Heran, W. J., Keane, T. M., & van der Kolk, B. A. (2001). Awareness under anesthesia and the development of posttraumatic stress disorder. *General Hospital Psychiatry, 23*, 198−204.

Owen, A. M., Coleman, M. R., Boly, M., Davis, M. H., Laureys, S., & Pickard, J. D. (2006). Detecting awareness in the vegetative state. *Science, 313*, 1402.

Pandit, J. J., Andrade, J., Bogod, D. G., Hitchman, J. M., Jonker, W. R., Lucas, N., Mackay, J. H., Nimmo, A. F., O´Connor, K., O'Sullivan, E. P., Paul, R. G., Palmer,

J. H. M. G., Plaat, F., Radcliffe, J. J., Sury, M. R. J., Torevell, H. E., Wang, M., Hainsworth, J., & Cook, T. M. (2014). 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. *British Journal of Anaesthesia, 113*, 549−559.

Phelan, L., Stargatt, R., & Davidson, A. (2009). Long-term posttraumatic effects of intraoperative awareness in children. *Pediatric Anesthesia, 19*, 1152−1156.

Revonsuo, A. (2006). *Inner presence: Consciousness as a biological phenomenon*. Cambridge, MA: MIT Press.

Revonsuo, A. (2010). *Consciousness: The science of subjectivity*. Hove & New York: Psychology Press.

Samuelsson, P., Brudin, L., & Sandin, R. H. (2008a). Intraoperative dreams reported after general anaesthesia are not early interpretations of delayed awareness. *Acta Anaesthesiologica Scandinavica, 52*, 805−809.

Samuelsson, P., Brudin, L., & Sandin, R. H. (2008b). BIS does not predict dreams reported after anaesthesia. *Acta Anaesthesiologica Scandinavica, 52*, 810−814.

Sanders, R. D., Tononi, G., Laureys, S., & Sleigh, J. (2012). Unresponsiveness ≠ unconsciousness. *Anesthesiology, 116*, 946−959.

Sebel, P. S., Bowdle, T. A., Ghoneim, M. M., Rampil, I. J. Padilla, R. E., Gan, T. J., & Domino, K. B. (2004). The incidence of awareness during anesthesia: A multicenter United States study. *Anesthesia and Analgesia, 99*, 833−839.

Simini, B. (2000). Awareness of awareness during general anaesthesia. *The Lancet, 355*, 672−674.

Sing Yi Eer, A., Padmanabhan, U., & Leslie, K. (2009). Propofol dose and incidence of dreaming during sedation. *European Journal of Anaestesiology, 26*, 833−836.

Stait, M. L., Leslie, K., & Bailey R. (2008). Dreaming and recall during sedation for colonoscopy. *Anaesthesia and Intensive Care, 36*, 685−690.

Tononi, G. (2009). Sleep and dreaming. In S. Laureys, & G. Tononi (Eds.), *The neurology of consciousness: Cognitive neuroscience and neuropathology* (pp. 89−107). London: Academic Press.

Tononi, G., & Laureys, S. (2009). The neurology of consciousness: An overview. In S. Laureys, & G. Tononi (Eds.), *The neurology of consciousness: Cognitive neuroscience and neuropathology* (pp. 375−412). London: Academic Press.

Wilson, S. L., Vaughan, R. W., & Stephen, C. R. (1975). Awareness, dreams, and hallucinations associated with general anesthesia. *Anesthesia and Analgesia, 54*, 609−617.

Xu, L., Wu, A.-S., & Yue, Y. (2009). The incidence of intra-operative awareness during general anesthesia in China: a multi-center observational study. *Acta Anaesthesiologica Scandinavica, 53*, 873−882.

Appendix

Coding instructions for subjective experiences during anesthesia

General instructions

Two judges individually assign each interview report according to the following scales. When two judges complete scoring individually, the assigned categories are compared, and inter-judge agreement is evaluated. In a case of disagreement, either the two judges discuss it further until agreement is achieved, or the third judge decides under which one of the suggested two categories a particular report or content should be placed in.

1. Report frequency and report type scale

The aim of this scale is to categorize all awakenings (awakening yes/no) and interview reports into those that contain anesthesia-related experiences and into those that do not. Anesthesia reports refer to reports that include anesthesia experiences that may have occurred after anesthesia induction, during the actual unresponsive period (LOR/LOC), or during unresponsiveness before the last awakening (recovery from LOC). Non-anesthesia reports refer to those reports that describe experiences that have taken place before anesthesia induction or after recovery, or to reports that do not include any kinds of experiences related to anesthesia session, for example participant reports what he remembers from his previous surgery experiences. A white report refers to occasions where the participant thinks he has had experiences during anesthesia, but cannot recall any content.

Coding instructions:

0 = No awakening

- The participant has not woken up after either LOR1 or LOR2 (ROR has not been achieved).

1 = Awakening but no report

- The participant has regained consciousness, but there is no report of any experiences, not even a white report.

2 = Non-anesthesia report (wake reports)

- A report including only experiences before anesthesia induction or after recovery of consciousness. Any sensations or perceptions, thoughts, emotions etc. reported from before the infusion has been started or after the participant woke up.
- For example, any mention of hearing sentences is coded into this category (training with 150 sentences during baseline), unless the participant indicates that even though he hears sentences, he cannot respond, etc.

3 = White report

- A report that states there were experiences during anesthesia (after infusion was started but before awakening), and the participant remembers something but no explicit content.

4 = Anesthesia report

- A report from during anesthesia, i.e. any sensations, perceptions, thoughts, emotions that have been experienced after infusion has been started but before the participant woke up. Can include experiences from after infusion, but before LOR (coldness in arm, the feeling of dizziness and tiredness) or from during LOR.
- For example, hearing the incorporation sound, or hearing sentences but being unable to move hands to respond, are categorized into anesthesia reports, as are dream-like imagery reports.

2. <u>Anesthesia report specific scale</u>

The aim of this scale is find out how many of the anesthesia-related reports include purely hallucinatory content, defined as internally generated experiences that are in no way related to the research environment or the experiment, from those that reflect memory incorporation of the research environment, and from those that reflect pure incorporation of stimuli that has been present only during LORs/LOC, and of which that participant has had no prior knowledge. To be scored, the report must be relatively clear, and ambiguous cases are not scored.

1. Dream-like experiences, hallucinations (anesthesia dreaming)

A participant reports having experienced a hallucinatory experience, i.e., reports content of consciousness that is not directly related to or does not originate from the research environment. Distorted experiences of the research environment, such as dreaming of a researcher in an imaginary environment, is scored as dreaming. The experience can be multimodal, or unimodal and static, even a thought-like experience. In case of ambiguity (e.g., one word unrelated to the rest of the report, unclear or meaningless sentences), dreaming is not scored.

2. Direct memory incorporation

A participant reports having had subjective experiences related to things/persons that have been present or events that have occurred during the anesthesia session, but the experiences may be memory incorporation from what the participant has experienced during wakefulness before the experiment was started (e.g., researchers in the room, researchers talking/whispering, monitors, computers, sentence stimuli, MMN stimuli, instructions) or from the very beginning of the experiment when the infusion has been started (e.g. feeling coldness in the arm, infusion pump noises, etc).

3. Awareness of the environment (anesthesia awareness)

A participant reports having had subjective experiences related to things/persons that have been present or events that have occurred during the anesthesia session, and these experiences are related to stimuli the participant cannot have expected to occur during the session (incorporation sound stimuli, lights flickering, announcements, problems with infusion, beeping of the anesthesia monitor, etc.)

3.1 Pure incorporations = true pure incorporation that are not related to arousal (such as reporting incorporation sounds)

3.2 Arousal related incorporations = incorporations that can be related to brief arousals (check log and EEG files!), such as recalling blood sampling, beeps (which in LOC can be related to recovery period and r-testing), sounds from the environment, the subject speaking himself (some participants spoke), moving around restlessly, snoring or waking up because of snoring, etc.

3. Orlinsky's Modified Scale for Perceptual Complexity and Dynamics of Dreams

Key concepts

Below are described several key concepts, which are essential during scoring of dream reports:

1) **Perceptual experience** is a defining characteristic of categories 1 and above. It is a relatively unique subjective experience in any of the sensory and perceptual modalities, e.g., seeing visual inanimate objects (e.g. book, room) and animate characters (e.g. dog, doctor); having auditory experiences (e.g. sound, music); having other sensory experiences, such as tactile, olfactory, pain, etc.

The following subjective phenomena should not be regarded as perceptual experiences (are coded as 0)

- thoughts (e.g. thinking about school);
- feelings and emotions (e.g. happiness);

Thus, reports containing only thoughts or emotions should be regarded as perceptually dreamless.

2) **Scene** is a defining characteristic of Complexity category 2 (and in many but not all cases also in category 3). It is a broader perceptual world in which other perceptual experiences are located. "Scene" is a relative concept and should be always defined by its relation to other perceptual experiences. If one bigger or broader percept includes another, smaller, percept, i.e., the smaller percept is encompassed by the bigger one, scene is scored. For instance, if two boys are reported to be playing in the school yard, school yard should be taken as a scene. Another important consideration is that subjects might assume and suggest the probable scene for percepts, e.g. "I think this should have happened at university". Such cases should be recognized and rejected as not being a scene and not falling under Category 2. For a report to be scored under Category 2, some perceptual experience should be reported that directly indicate the presence of a scene, e.g. "This happened at university, I saw a corridor and doors to the seminar room".

3) **Change** is a defining characteristic of category 3. Change can occur between unconnected or interconnected percepts, without the presence of a scene. Change might take place, when (1) one entity of the report − sound, visual object or interacting character − is replaced by another; (2) a new entity enters the report; or (3) a previously present entity disappears. A more substantial change happens when the whole scene of a dream is replaced by another surrounding, e.g. "We were in school, later we went to the cinema".

Motion that does not lead to the emergence of new perceptual entities or to the development of dream story is not counted as a change. Thus, repetitive actions (e.g. "We were walking in the forest", "She was writing a letter") are excluded from the concept of change. However, the appearance or disappearance of simple and / or repetitive actions would signal the presence of change, e.g. "We were walking in the forest and suddenly stopped", "She was writing a letter, but pencil dropped down".

Simplified Orlinsky Scale

Static percepts

Category 1 = An isolated, fragmentary percept OR several unconnected or interconnected percepts are reported, but there is **no** perceptual information given about a more general **scene** in which the experiences do happen.

Static scene with objects

Category 2 = Scene is defined as one percept encompassing another. Thus, when a bigger percept includes or encompasses a smaller one, this is scored under category 2. The scene may also change, but there is no change within a single scene.

Dynamic percepts

Category 3 = Some change occurs between several interconnected experiences OR change happens between interconnected experiences within a scene or between scenes.

Special cases

Below are discussed several cases that might be problematic during scoring:

1) Adjectives related to particular external objects (e.g. "there was a *nice* dog") are not counted as separate objects.

2) Perceptual experiences of plural entities (e.g. "trees"; "stream of musical sounds") should be counted as two interconnected experiences.

3) If spatially larger percept includes a smaller one (e.g. "doors in the room"; "picture on the doors"), this is counted as a scene.

4) Typically, Self in a dream is not counted as a separate perceptual experience. However, seeing oneself from outside or just some parts of a body from inside (e.g. "then I looked at my hands"), having explicit or implicit tactile sensations (e.g. "I felt cold in my legs", "I was keeping a book in my hands"), having motivational states (e.g. "I was very hungry") are counted as perceptual experiences.

4. The Modified Subjective Experiences During Anesthesia Scale

This scale consists of categories for basic subjective experiences from any of the phenomenal modalities, from sensation to affective states to thinking. A single report may include a large number of separate experiences from different modalities, and each experience is coded separately.

1. Sensory-perceptual experiences

A participant reports having had sensory-perceptual experiences in visual, auditory, sensorimotor, olfactory and gustatory modalities.

1.1 Visual experiences may vary from experiencing very basic visual qualities, for example light, shape or motion, to seeing highly complex visual scenes, for example people, houses or medical equipment.

1.2 Auditory experiences range from meaningless sounds, for example background noise, to very complex sounds, for example music or language.

1.3 Interoceptive experiences include internal motivational states, for example hunger or thirst.

1.4 Tactile experiences, includes all tactile experiences, excluding pain.

1.5. Pain and temperature, includes all sensations related to pain, heat, coldness, etc.

1.6. Kinesthetic experiences, for example experiences of movement or vestibular experiences like explicit sensation of body position, equilibrium or disbalance.

1.7 Olfactory experiences include all types of smells.

1.8 Gustatory experiences include all types of tastes, for example experiences related to eating.

2 Affective states; moods, feelings

A participant reports having had emotions, feelings or moods.

2.1 Positive affective state includes joy, pleasure, excitement, tranquility, relaxation, etc.

2.2 Negative affective state includes anxiety, panic, disturbance, fear, etc.

3 Cognition

A participant reports having had inner speech or, thinking. This category includes cognitive phenomena that happen 'inside' a participant's head − voluntarily or involuntarily thoughts (such as 'inner speech'), remembering, planning, and silent reflection of the content in phenomenal consciousness. Sentences in reports starting with words such as 'I thought/I remembered/I doubted/I considered/I planned/I concluded/I realized/I understood/I knew that…', 'I was sure that…', 'I was interested…', 'I wondered', could indicate the presence of thought-like experiences.

4 Out of body experiences

A participant reports having observed the self body and / or the laboratory situation from an outsider position.

5 Sense of presence

A participant reports a sense of presence.

Svensk sammanfattning – Swedish summary

Subjektiva upplevelser vid anestesi som framkallats av dexmedetomidine eller propofol

Inledning

Under de tre sista årtiondena har medvetandestudier vuxit till ett livskraftigt forskningsområde inom den moderna forskningsvärlden (Revonsuo, 2010). Det har sedan länge funnits olika filosofiska teorier om medvetandets egentliga natur som nu håller på att bli empiriskt testade. Det grundläggande syftet med dessa empiriska undersökningar är att koppla individens subjektiva upplevelser samt yttre beteende till neurala motsvarigheter i hjärnan. Det är av stor vikt hur man definierar medvetandet och dess neurologiska och beteendemässiga markörer när man genomför dylika undersökningar. Det har redan visat sig att relationen mellan medvetande och dess yttre markörer, så som reaktivitet, inte alls är lineär (t.ex. Owen et al., 2006). Ett exempel på detta är de subjektiva upplevelser som patienter ibland rapporterar efter kirurgiska operationer vid anestesi även om de till synes inte har varit vid medvetande. Även nedsövda patienter inte reagerar på sin omgivning, är det ändå möjligt att de drömmer eller, vilket är mera sällsynt, är medvetna om sin omgivning och även om själva operationen under anestesiperioden.

Ett fenomen som är relaterat till medvetande och anestesi är medvetenhet vid anestesi (anesthesia awareness), det vill säga en situation där den nedsövda patienten är medveten och förmögen att uppleva yttre stimuli, men oförmögen att utrycka det på något sätt och är med andra ord oresponsiv. Vid kirurgisk anestesi förhindras responsivitetet i allmänhet av muskelrelaxanter, men efter operationen kan patienter rapportera upplevelser eller händelser som härstammar från anestesiperioden. Medvetenhet under anestesi är ändå ett väldigt sällsynt fenomen och mycket forskning har ägnats åt det på senaste tiden. Frekvensen för fenomenet är enligt de flesta studierna ca 0.10−0.14 % (Mashour et al., 2012; Samuelsson et al., 2008a; Sebel et al., 2004) i västvärlden, även om en senare nyligen genomförd studie visade en betydligt lägre frekvens, 0.005 % (Pandit et al., 2014).

En annan upplevelse som kan förekomma vid anestesi är drömmande som i det här sammanhanget definieras som en erfarenhet man kommer ihåg som inte är medvetenhet och som har tagit plats mellan anestesi induktion och tidpunkten då man kommer ut ur anestesin och medvetandet återvänder (Hobbs et al., 1988). Forskningsresultat har visat att ungefär en femtedel av patienter rapporterar drömmande under anestesiperioden då de intervjuas direkt efter uppvaknandet (Leslie et al., 2007; Brandner et al., 1997), även om siffrorna kan variera betydligt mellan undersökningar, t.ex. från 6 % (Leslie et al., 2005) till 53 % (Errando et al., 2008). I en experimentell studie av Noreika et al. (2011), som genomfördes med friska unga deltagare som var nedsövda med bara ett anestesiläkemedel, var frekvensen av drömmandet 59 %. De rapporterade drömmarna vid anestesi tenderar vara korta och behagliga till naturen och ha med det vardagliga livet att göra (Leslie & Skrzypek, 2007; Aceto et al., 2007; Kim et al., 2011). Det finns endast ett fåtal undersökningar när det kommer till innehållet av drömmar vid anestesi eller av de tankar som patienter har vid medvetande vid anestesi. I praktiken är den enda omfattande innehållsanalysen genomförd i en experimentell studie av Noreika et al. (2011), i vilken Subjective Experiences During Anaesthesia Coding System (SEDA-skalan) användes.

I vår studie försökte vi undvika de metodologiska fallgroparna som har funnits i tidigare studier som undersökt medvetande vid anestesi och drömmande vid anestesi. I denna studie sövdes friska unga deltagare ned med endast ett anestesiläkemedel, antingen med propofol eller med dexmedetomidine i ett rent experimentellt upplägg. Inga ytterligare medicineringar eller anestesiläkemedel användes. För att få en tydligare bild av ovannämnda fenomen vid anestesi intervjuades deltagarna både under och efter anestesiperioden, vilket möjliggjorde att man kunde definiera om de rapporterade subjektiva upplevelser härstammade från själva anestesiperioden eller från återhämtningsperioden, som följer avslutningen av infusionen. Därtill utfördes en omfattande innehållsanalys av rapporterna om de anestesirelaterade subjektiva upplevelserna.

Metod och material

Den här studien var utförd som en del av ett projekt vid namnet Conscious Mind, vilket är en omfattande experimentell studie som undersöker förändringar i hjänrnaktivitet i relation till anestesi och naturlig sömn. Varierande mätinstrument har används i projektet, så som elektroenkefalografi (EEG), positronemissionstomografi (PET) och funktionell magnetresonanstomografi (fMRI), och försöksdeltagarnas retrospektiva rapporter har använts för att studera subjektiva upplevelser vid anestesi eller sömn.

Sammanlagt 47 friska manliga frivilliga försökspersoner mellan åldern 20 till 30 år deltog i studien. Två olika anestesiläkemedel, propofol eller dexmedetomidine, administrerades slumpmässigt till försökspersonerna (propofol *n* = 24, dexmedetomidine *n* = 23). Dosen av anestesiläkemedlet höjdes gradvis tills försökspersonen uppnådde ett oresponsivt tillstånd (LOR = loss of responsiveness). Tillståndet kontrollerades med närvaro eller frånvaro av respons till auditiva stimuli genom att pressa på handtag. Efter en oresponsiv period som omfattade ca 25 minuter (LOR1), försökte försökspersonen väckas och de som vaknade (ROR1 = return of responsiveness) intervjuades. Efter intervjun stimulerades försökspersonen inte och ifall han återvände till ett oresponsivt tillstånd med samma dos av narkosläkemedlet, repeterades proceduren (LOR2, ROR2 & intervju). Därefter, eller ifall LOR2 inte lyckades, höjdes dosen 1.5 gånger för att säkra en förlust av medvetandet (LOC = loss of consciousness). Efter att den anestetiska infusionen avslutades och efter att försökspersonen antingen själv hade vaknat eller blivit väckt (efter 30 min) intervjuades han igen (ROR3). Intervjuerna transkriberades, klassificerades och analyserades av två av varandra oberoende bedömare i flera faser. Först separerades rapporter som inkluderade upplevelser från anestesiperioden från de som inte inkluderade dylika upplevelser. Sedan kategoriserades de anestesirelaterade upplevelserna utgående ifrån ifall de innehöll drömliknande, hallucinatoriskt material, direkta minnesbilder från experimentet eller medvetande om omgivningen, dvs. minnen om händelser från anestesiperioden som försökspersonen inte kunde ha vetskap om. Sedan graderades de subjektiva upplevelsernas komplexitet med hjälp av Orlinskys (1962) modifierade skala, och dessutom kartlagdes det perceptuella innehållet.

Resultat

Interbedömarreliabiliteten evaluerades med procent överensstämmelse och Cohen's Kappa koefficient och den var relativt hög under hela bedömningsprocessen, 88.5%-98.8 % och från $K = 0.76$ till 0.97 ($p < .001$).

Antalet framgångsrika väckningar under anestesiperioden (ROR1 & ROR2) var signifikant högre hos deltagare som fick dexmedetomidine jämfört med de deltagare som fick propofol ($p < .05$, Fisher's Exact Test). Därtill kunde signifikant färre deltagare som fått propofol och som vaknade i LOR1 återvända till det oresponsiva tillståndet ($p < .05$). De flesta väckningarna ledde med båda anestesiläkemedlen till en rapport som inkluderade anestesirelaterade upplevelser, men vid sista väckningen (ROR3) rapporterade deltagare som fick dexmedetomidine signifikant flera anestesirelaterade upplevelser än de som var nedsövda med propofol (95.7 % vs. 72.7 %, $p < .05$).

När deltagaren rapporterade subjektiva upplevelser relaterade till anestesin, var drömmande (det vill säga internt skapade hallucinatoriska subjektiva upplevelser icke-relaterade till studiemiljön) det mest rapporterade innehållet vid båda narkosmedlen. Där fanns dock en signifikant skillnad mellan medlen vid första väckningen (ROR1) då deltagare som sövts ned med dexmedetomidine rapporterade flera drömmar än de som fick propofol (100 % vs. 62.5 %, $p < .05$). Direkta minnesbilder från studiemiljön var även vanliga vid båda medlen. Däremot var rapporter som inkluderade medvetenhet om omgivningen, det vill säga minnesbilder av händelser från undersökningsmiljön som försökspersonen varken kunde ha vetskap om eller kunde ha förväntat sig att ha tagit plats under LOR eller LOC, var sällsynta och hände alltid i samband med korta uppvaknanden.

Perceptuell komplexitet kodades skilt för drömliknande upplevelser, minnesbilder och medvetenhet om omgivningen med en modifierad version av Orlinskys skala (1962). Majoriteten av alla rapporter som kodades i detta skede hade perceptuellt innehåll i alla stadier av anestesin (86.4−100.0 %). Komplexiteten hos drömliknande upplevelser var ganska jämt distribuerad mellan de tre nivåerna (static, scene & dynamic) i alla stadier, medan majoriteten av minnesbilder och medvetenhet-upplevelser var statiska till naturen. Det fanns inga signifikanta skillnader mellan anestesiläkemedlen gällande komplexiteten av perceptuella upplevelser.

Perceptuella innehållet kodades också separat för drömliknande upplevelser, minnesbilder och medvetenhet om omgivningen. Majoriteten av drömliknande upplevelser innehöll visuellt material i alla stadier av anestesin (81.8−93.9 %), medan andra upplevelser rapporterades mindre rikligt, så som auditiva och kognitiva (< 42.4 %). Majoriteten av minnesbilderna innehöll auditiva upplevelser (56.7−75.0 % i alla stadier), medan visuella upplevelser var närvarande men mer sällsynta (25.0−46.7 %). Det flesta av de få medvetenhet-rapporterna inkluderade auditiva upplevelser (8/13).

Diskussion

Syftet med denna studie var att undersöka subjektiva upplevelser i ett oresponsivt tillstånd som skapades genom att ge försökspersoner anestesiläkemedlen dexmedetomidine eller propofol. Ett nytt metodologiskt närmandesätt användes i jämförelse med tidigare studier inom ämnesområdet, det vill säga deltagarna väcktes under anestesiperioden för att noggrannare kartlägga tidpunkten av de subjektiva upplevelserna. Dessutom användes ett omfattande kodningssystem för att mer exakt kunna definiera innehållet av subjektiva upplevelser under anestesi.

Frekvensen av drömmande var högre i denna studie i jämförelse med flera tidigare studier, närmare sagt mellan 80 % och 88 % beroende på tidpunkten för väckningen. Majoriteten av studier som undersökt drömmande vid anestesi har rapporterat att ungefär en femtedel av patienter drömmer vid anestesi (Leslie et al., 2007; Brandner et al., 1997). Dock har de flesta studier genomförts i en klinisk omgivning i samband med kirurgiska operationer i vilka ett flertal läkemedlen har använts och intervjuerna har gjorts efter spontan återhämtning, vilket kan förklara den lägre frekvensen av drömmande i jämförelse med denna studie. Däremot är resultat av denna studie i enlighet med resultat från en studie av Noreika et al. (2011) som genomfördes i liknande omständigheterna och som uppvisade en frekvens av drömmande på 59 %.

Rapporterna från anestesin som försökspersonerna gav i denna studie innefattade perceptuella innehåll i de flesta fall i alla väckningarna (86 −100 %). Även om komplexiteten av det rapporterade drömliknande innehållet var ungefär jämt fördelad, var dynamiskt material närvarande i bara 18.2 % (ROR1) till 33.3 % (ROR3) av fallen, vilket verkar stöda Leslie och Skrzypeks (2007) syn på att anestesi drömmar är enkla till naturen.

Rapporterna om medvetenhet om omgivningen under anestesiperioden var sällsynta i vår studie och de var alltid kopplade till korta uppvaknanden som upptäcktes i EEG, vilket stöder tidigare studiers resultat som visat hur ovanligt fenomenet faktisk är (t.ex. Mashour et al., 2012; Samuelsson et al., 2008a; Sebel et al., 2004).

Ifrågavarande studie har en del begränsningar som bör nämnas. Det relativt knappa antalet försökspersoner kom speciellt till synes i faserna ROR1 och ROR2, i vilka betydligt färre försökspersoner som fått propofol kunde väckas och ge rapporter, vilket försvårade jämförelsen av rapporterna mellan de två anestesiläkemedlen. När det gäller väckningarna under anestesins gång var också några försökspersoner antingen väldigt sömniga (dexmedetomidine) eller desorienterade (propofol), vilket ibland försvårade utförandet av intervjun.

Den här studien är i enlighet med andra tidigare studiers fynd gällande drömmande och medvetenhet vid anestesi som visat att närvaro eller frånvaro av medvetna upplevelser vid anestesi inte nödvändigtvis kan bedömas på basis av yttre signaler. Även om försökspersonerna var i ett oresponsivt tillstånd till följd av en liten dos av antingen dexmedetomidine eller propofol, rapporterade de subjektiva upplevelser i samband med väckningar under och efter den anestetiska infusionen i ett experimentellt upplägg. Drömliknande erfarenheter rapporterades oftast, men också minnesbilder av undersökningsmiljön var vanliga i rapporterna. Däremot var medvetenhet om omgivningen sällsynt och kopplad till korta uppvaknanden. Rapporter givna under den anestetiska infusionen påvisade att subjektiva upplevelser inte bara härstammar från återhämtningsperioden som följer avslutningen av den anestetiska infusionen. Sammanfattningsvis, även om individen är oresponsiv, så orsakar lätt experimentell anestesi inte nödvändigtvis omedvetenhet, dvs. frånvaro av subjektiva upplevelser.

PRESSMEDDELANDE

Medvetenhet under anestesi kan inte dömas enligt yttre signaler

Pro gradu-avhandling i psykologi, Fakulteten för humaniora, teologi och psykologi, Åbo Akademi

Resultaten från en pro gradu-avhandling vid Åbo Akademi visar att medvetenhet vid anestesi inte kan dömas enligt yttre signaler. Milla Karvonen har undersökt subjektiva upplevelser vid anestesi inom ramen för det tvärvetenskapliga projektet ”Conscious Mind” som utförts vid Åbo universitet. Då man sövde ned friska deltagare med ett anestesiläkemedel i experimentellt syfte, rapporterade de flesta vid uppväckning upplevelser som var relaterade till anestesin under och efter infusionen (83 %). Majoriteten av upplevelserna var drömliknande (85 %), medan medvetenhet om omgivningen var sällsynt och alltid relaterad till korta uppvaknanden. Det drömliknande materialet som rapporterades var till sin natur relativt enkelt och för det mesta visuellt (89 %).

Detta indikerar enligt Karvonen att även om individer blivit nedsövda med små doser av ett anestesiläkemedel i ett experimentellt upplägg inte reagerar till yttre stimuli, betyder det nödvändigtvis inte att de är medvetslösa, det vill säga inte har några subjektiva upplevelser alls. Genom att väcka och intervjua deltagarna under anestesiperioden kunde man för första gången visa att anestesirelaterade upplevelser inte härstammar bara från återhämtningsperioden som följer efter att anestesin avslutats.

Sammanlagt deltog 47 unga män i studien, varav 24 var nedsövda med propofol och 23 med dexmedetomidine. Försökspersonerna intervjuades om deras subjektiva upplevelser både vid anestesin och efter den. Intervjuerna analyserades därefter enligt skalor som var specifikt designade för kodning av upplevelser vid anestesi.

Ytterligare information fås av:

Milla Karvonen, FM, magisterstuderande i psykologi, Psykologi/Åbo Akademi, 044 3000 529, mikarvon@abo.fi

Katja Valli, Docent, Centret för kognitiv neurovetenskap, Psykologi/Åbo universitet, katval@utu.fi

Petra Grönholm-Nyman, FD, universitetslärare, Psykologi/Åbo Akademi, 02 215 4737, pegronho@åbo.fi