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Research Article

Dreaming and awareness during dexmedetomidine- and propofol-induced unresponsiveness

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Background: Experiences during anaesthetic-induced unresponsiveness have previously been investigated by interviews after recovery. To explore whether experiences occur during drug administration, we interviewed participants during target-controlled infusion (TCI) of dexmedetomidine or propofol and after recovery.
Methods: Healthy participants received dexmedetomidine (n=23) or propofol (n=24) in stepwise increments until loss of responsiveness (LOR1). During TCI we attempted to arouse them for interview (return of responsiveness, ROR1). After the interview, if unresponsiveness ensued with the same dose (LOR2), the procedure was repeated (ROR2). Finally, the concentration was increased 1.5-fold to achieve presumable loss of consciousness (LOC), infusion terminated, and the participants interviewed upon recovery (ROR3). An emotional sound stimulus was presented during LORs and LOC, and memory for stimuli was assessed with recognition task after recovery. Interview transcripts were content analysed.
Results: Of participants receiving dexmedetomidine, 18/23 were arousable from LOR1 and LOR2. Of participants receiving propofol, 10/24 were arousable from LOR1 and two of four were arousable from LOR2. Of 93 interviews performed, 84% included experiences from periods of unresponsiveness (dexmedetomidine 90%, propofol 74%). Internally generated experiences (dreaming) were present in 86% of reports from unresponsive periods, while externally generated experiences (awareness) were rare and linked to brief arousals. No within drug differences in the prevalence or content of experiences during infusion *vs* after recovery were observed, but participants receiving dexmedetomidine reported dreaming and awareness more often. Participants receiving dexmedetomidine recognised the emotional sounds better than participants receiving propofol (42% *vs* 15%), but none reported references to sounds spontaneously.

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Conclusion: Anaesthetic-induced unresponsiveness does not induce unconsciousness or necessarily even disconnectedness.
Clinical trial registration: NCT01889004.

Keywords: awareness; consciousness; dexmedetomidine; interview; propofol

Editor's key points

- The frequency and drug dependence of dreaming and awareness during infusion of i.v. anaesthesia have not been carefully studied under controlled conditions.
- Healthy male volunteers rendered unresponsive with target controlled infusion of dexmedetomidine or propofol were awakened and subjected to semi-structured interviews.
- Dreaming during unresponsiveness was frequent with both drugs, while awareness was rare.
- Dexmedetomidine or propofol titrated to induce behavioural unresponsiveness frequently do not abolish conscious experiences or even necessarily induce disconnectedness.

The content of consciousness, i.e. subjective experiences, can be either externally or internally generated. Being able to have externally generated experiences implies that the person is, at least momentarily, in a state of connected consciousness. In contrast, when externally generated contents of consciousness cannot occur, but purely internally generated contents of consciousness are present, the person is in a state of disconnected consciousness. In general anaesthesia, intraoperative awareness with explicit recall implies connectedness to the environment, while internally generated experiences, often conceptualised as dreaming in anaesthesia literature, are typically interpreted to represent a disconnected conscious state.[1,2]

Most studies on subjective experiences under anaesthesia have been conducted in a clinical setting. In previous studies, the incidence of awareness has ranged from 0.007% to 1.0%.[3] Similarly, the incidence of dreaming has varied greatly, from 3.2% to 52.6%[4–9] when patients have been interviewed after recovery from general anaesthesia. After sedation, 19.0% have reported dreaming.[10] However, the length and depth of anaesthesia, the patient's clinical condition, and the combination of anaesthetics and other medications can affect the presence and later recall of experiences.[11] The only single-drug experimental study found that 58.6% of participants reported experiences after spontaneous emergence from unresponsiveness induced by dexmedetomidine or propofol, of which 26.3% included dream-like imagery and 38.6% references to the research setting.[11] However, a common bias to previous studies is that participants have been interviewed after a recovery period. In fact, it has been suggested that dreaming occurs after termination of drug administration before awakening when patients are sedated or in a physiological sleep state.[5,12,13] As it remains unresolved whether the reported experiences originate from the drug administration period or the recovery-phase with only minimal drug concentrations, we conducted interviews by arousing healthy participants from unresponsiveness during target-controlled infusion (TCI), and upon recovery after terminating drug administration. We defined internally generated experiences as dreaming (implying disconnected consciousness), and externally generated experiences as accurate awareness of the research environment (implying connectedness). Based on the suggestion that dreaming occurs during recovery,[5,12,13] we hypothesised dream experiences to be more prevalent in recovery reports than in reports obtained during infusion. To measure awareness of specific stimuli, participants were also presented with emotional sound stimuli during unresponsiveness followed by a recognition task after recovery.

Methods

The protocol was approved by the Ethics Committee of the Hospital District of Southwest Finland, and the Finnish Medicines Agency Fimea, and registered in ClinicalTrials.gov (NCT01889004). Written informed consent was acquired from the participants according to the Declaration of Helsinki. Spectral analysis of the EEG and event related potentials from the same study are reported elsewhere.[14–15]

Participants

Forty-seven non-smoking, 20–30-yr-old, right-handed healthy male subjects (ASA physical status I) with normal hearing participated in this open-label, randomised (permuted blocks) parallel-group (n=23 for dexmedetomidine and n=24 for propofol) study. Participants were recruited from the local universities by advertising in student mailing lists, and they were paid €150 (approved by the Ethics Committee). Only males were considered eligible because of radiation exposure related to a subsequent positron emission tomography study. No statistical power calculation regarding the required number of participants was conducted before the study, but the sample size was based on our previous experience with this design. Participants' mean age was 24 (range 20–30) yrs, mean height was 180 (range 165–198) cm and mean weight 78 (range 53–122) kg. Fulfilment of exclusion criteria (smoking, history of psychiatric disorder, propensity for nausea, substance abuse) was verified by prestudy interview and laboratory screening.

Anaesthetic protocol

The anaesthetic procedure (as described in[14]) was conducted by a resident and an experienced senior an aesthesiologist was always present. Medication and alcohol use were forbidden for 48 h preceding the experiment, and participants fasted overnight. Vital signs were monitored and step-wise increasing concentrations of either dexmedetomidine or propofol were administered using TCI until loss of responsiveness (LORs) was achieved. For dexmedetomidine, the starting target plasma concentration was 1.0 ng ml^{-1}, followed first by a 0.5 ng ml^{-1} target concentration increase and 0.25 ng ml^{-1} increases thereafter. For propofol, the starting target plasma concentration was 1.0 μg ml^{-1}, followed first by a 0.5 μg ml^{-1}