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EVALUATION OF COGNITIVE FUNCTIONS AFTER SURGERY ACCORDING TO TWO TYPES OF ANAESTHESIA (HYPNOSEDATION OR CONVENTIONAL GENERAL ANAESTHESIA) IN PATIENTS UNDERGOING SURGERY FOR BREAST CANCER

HYPNOSEIN PROTOCOL

SYNOPSIS

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SYNOPSIS

Study title	**Evaluation of cognitive functions after surgery according to two types of anaesthesia (hypnosedation or conventional general anaesthesia) in patients undergoing surgery for breast cancer**
Acronym	**HYPNOSEIN**
Sponsor	**Institut Bergonié** **Centre de Lutte Contre le Cancer (CRLCC)** **229 Cours de l'Argonne** **33076 Bordeaux Cedex**
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Number of centres	3 centres: ▪ Institut Bergonié (Sponsor) ▪ Strasbourg (CRLCC) ▪ Lille (CRLCC)
Indication	Patients with breast cancer requiring breast surgery
Study justification	The onset of cognitive disorders after surgery under general anaesthesia (GA) is the second cause of patient complaints (after dental injury caused by intubation techniques). These cognitive disorders can range from simple reversible confusion (26%) to post-operative cognitive dysfunctions without actual recovery (10%). Hypnosedation is an old anaesthesia technique which is fast-growing, of which the effects on cognitive functions remain unknown, but appear to be promising.
Expected results	The safety of hypnosedation, which uses anaesthetic drugs at doses ten times lower than those used during general anaesthesia, could be demonstrated on cognitive functions, and thus become an anaesthetic alternative, in certain types of surgery, in patients at risk of post-operative cognitive dysfunction.
Objectives	**Primary objective:** Evaluate the change in cognitive functions in patients treated for breast cancer by surgery, according to the type of anaesthesia chosen by the patient: hypnosedation or conventional general anaesthesia. **Secondary objectives:** Evaluate the characteristics of patients (physiological, mental and sociocultural) according to the type of anaesthesia selected, in order to identify characteristics likely to predict the choice of hypnosedation. According to the type of anaesthesia, evaluate the following, before and after surgery: pain, level of anxiety and patient satisfaction with the anaesthesia technique.
Study design	Observational, prospective, exploratory, multicentric study in 2 groups, according to the type of anaesthesia selected: hypnosedation or general anaesthesia
Number of patients	50 assessable patients (25 in each group)
Inclusion criteria	▪ Females, age 18 to 80 years, ▪ Confirmed breast cancer diagnosis (positive pathology test), ▪ Life expectancy greater than 6 months, ▪ Breast tumour resection with or without lymph node removal, mastectomy with or without lymph node removal, isolated lymph node removal,

	▪ ASA 1 (patient in normal health) or 2 (patient with mild systemic disease) according to the classification by the American Society of Anesthesiologists, ▪ Affiliation to a social security scheme, ▪ Subject informed and informed consent form signed
Exclusion criteria	▪ Presence of major psychotic psychiatric disorders or addictive behaviour, evaluated by the neuropsychologist at the first preoperative consultation, using the MINI test (MINI > 4 positive responses for each module) ▪ Presence of treated or untreated known neurological disorders, evaluated by the neuropsychologist at the first preoperative consultation, using the MMSE test (MMSE < 24) ▪ Patients on oral morphine for longer than 3 months, ▪ Pregnant or breastfeeding patients, or patients of childbearing age not using the appropriate contraception, ▪ Patient included in another clinical study, ▪ Subjects unable to undergo medical follow-up during the trial for geographical, social or psychological reasons, ▪ Patients deprived of freedom and adults subject to legal protection measures or unable to give their consent.
Study procedure	▪ **Screening visit: Pre-anaesthesia consultation (more than 48h before surgery)** The anaesthetist checks the inclusion and exclusion criteria and describes in detail the two management methods proposed by the study. An information document and consent form is handed to patients. ▪ **Preoperative consultation (D – 1: day before surgery)** On admission, the patient meets with the anaesthetist who ensures they have the patient's consent to participate and that they have signed an informed consent document, before they are referred for the neuropsychological consultation. After the eligibility consultation, the patient is confirmed or not, based on the results of the MINI and MMSE tests. ▪ **Inclusion visit: pre-anaesthesia visit: inclusion** The anaesthetist informs the patient of the results of the neuropsychological consultation and whether she meets the eligibility criteria. They question the patient on the type of anaesthesia chosen, either general anaesthesia or hypnosedation. This information is recorded on the inclusion form that the anaesthetist forwards to the Clinical Research Associate in charge of the study. ▪ **Per- and post-operative analgesic protocol (regardless of the type of anaesthesia)** Slow direct intravenous injection of Proparacetamol / 6 h and slow direct intravenous injection of Ketoprofen / 8 to 12 h, and morphine if the numerical scale is ≥ 4. Follow-on oral analgesic treatment with paracetamol and ibuprofen. ▪ **Hypnosedation protocol** Patients receive Alprazolam 0.25 premedication 1 hour before surgery. The anaesthetist begins induction of hypnosis by asking the patient to close her eyes or to stare at a specific point. They continue with bodily relaxation and work on

	breathing; at the same time, they begin sedation with a morphinic (remifentanyl 0.05γ/kg/min to 0.1γ/kg/min) and midazolam (0.5 to 1.5 mg). The surgeon administers the local anaesthetic which is a mixture of 10 cc xylocaine 2% and 10 cc marcaine 0.5%. The anaesthetist deepens the trance by suggesting the happy memory chosen beforehand by the patient, and remains constantly in contact with the patient, and also the surgeon, as mediator between the two. From the start of closure of the surgical wound, the anaesthetist stops sedation and gradually brings the patient out of her hypnotic state. ▪ **General anaesthesia protocol** After pre-oxygenation with the face mask for 5 min, anaesthesia induction and maintenance take place according to standard practice, using propofol and remifentanyl by TCI (target-controlled infusion), the airways being controlled by a laryngeal mask or intubation tube, and drug administration being stopped on dressing placement. ▪ **Surgery** The standard surgeries concerned are breast tumorectomy with or without lymph node removal, mastectomy with or without lymph node removal, isolated lymph node removal, tumorectomy or even mastectomy with sentinel lymph node identification, sentinel lymph node isolated identification. ▪ **Immediate post-operative assessment (D1 to D7) and check-up (1 month later)** • Evaluations of cognitive functions by the neuropsychologists • Pain, anxiety, morphine treatments by the anaesthetist/resuscitator
Endpoints	We will evaluate cognitive disorders with a series of validated neuropsychological tests, including a cognitive complaint questionnaire for subjective cognitive disorders, and Grober and Buschke memory test, attentional tests and executive function tests for objective cognitive disorders. Pain and satisfaction in patients will be assessed using a numerical scale, and emotional state using the HAD scale.
Statistical analyses	The scores for each of the tests concerning subjective and objective cognitive function disorders and assessment of pain and anxiety will be described using descriptive statistics (mean, median, minimum and maximum) and graphs, at the 3 assessment intervals (preoperative, immediately after surgery and one month after surgery), <u>overall and according to the type of anaesthesia.</u>
Schedule	▪ Start of inclusions: March 2010 ▪ Inclusion phase: March 2010 to February 2012 ▪ Participation time of each patient: 1 month ▪ Total study duration: 2 years and 1 month