UNIVERSITAT ROVIRA I VIRGILI

HYPNOSIS VERSUS ANESTHESIA: A STUDY WITH CHILDREN UNDERGOING MAGNETIC RESONANCE IMAGING PROCEDURES

Marialuisa Malafronte

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Marialuisa Malafronte

Hypnosis versus Anesthesia: a study with children undergoing Magnetic Resonance Imaging Procedures

DISSERTATION THESIS

Supervisor

Prof. Dr. Jordi Miró

Department of Psychology

UNIVERSITAT ROVIRA I VIRGILI

Tarragona, 2021

UNIVERSITAT ROVIRA i VIRGILI

FAIG CONSTAR que aquest treball, titulat "Hypnosis versus Anesthesia: a study with children undergoing Magnetic Resonance Imaging Procedures.", que presenta Marialuisa Malafronte per a l'obtenció del títol de Doctor, ha estat realitzat sota la meva direcció al Departament de Psicología d'aquesta universitat.

HAGO CONSTAR que el presente trabajo, titulado "Hypnosis versus Anesthesia: a study with children undergoing Magnetic Resonance Imaging Procedures", que presenta Marialuisa Malafronte para la obtención del título de Doctor, ha sido realizado bajo mi dirección en el Departamento de Psicologia de esta universidad.

I STATE that the present study, entitled "Hypnosis versus Anesthesia: a study with children undergoing Magnetic Resonance Imaging Procedures", presented by Marialuisa Malafronte for the award of the degree of Doctor, has been carried out under my supervision at the Department Psychology of this university.

Reus, 26 de febrer de 2021

El/s director/s de la tesi doctoral
El/los director/es de la tesis doctoral
Doctoral Thesis Supervisor/s

[Dr. Jordi Miró Martínez]

UNIVERSITAT ROVIRA I VIRGILI

This is to certify that:

The Present Dissertation: *Hypnosis versus Anesthesia: a study with children undergoing Magnetic Resonance Imaging procedures*, presented by Marialuisa Malafronte, has been supervised by Dr. Jordi Miró Martínez, Professor at the Department of Psychology of the Universitat Rovira i Virgili, in Fulfillment of the Requirements for the degree of Doctor of Philosophy.

Tarragona, 2021

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Jordi Miró Martínez, PhD

Considerate la vostra semenza:

Fatti non foste a viver come bruti ma a seguir vertute e conoscenza

Consider well the seed that gave you birth: you were not made to live as beasts, but to follow virtue and knowledge.

Inferno Canto XXVI

Dante

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INDEX

I. INTRODUCTION

The structure of the thesis

This thesis is composed of two sections. The first section is a theoretical analysis, which includes an introduction to hypnosis and pharmacological anesthesia, a literature overview about the use of hypnosis in the anesthesia field, and at the end, a specific focus on the area that was deepened by our study: the use of hypnosis in an MRI setting in pediatrics.

The second section gives a complete description of the study procedures and includes objectives, methods (divided into the following sections: "Participants," "Procedures," "Measures"), results, discussion, and conclusions. A final section, named "Supplementary materials," has been included. This section describes the findings in functional studies that would help us better understand the nature of hypnosis and pharmacological anesthesia.

INTRODUCTION

1. Synopsis

The term "anesthesia" derives from "an" (privative meaning) and "àisthesis" (sensation). It indicates: (1) the lack of sensitivity of the body or a part of it; (2) the elimination of sensitivity and (3) the medical practice that has this effect.

All the techniques (e.g., general and local pharmacological anesthesia, hypnosis, the use of herbs such as mandragora or opium) that can produce the aforementioned effects can be called anesthesia. These techniques have changed over time and the development of knowledge.

One of the oldest techniques used as anesthesia is hypnosis: "induction of a subjective state in which alterations of perception or memory can be elicited by suggestion" (Wobst, 2007, p.1199).

With the discovery of ether and chloroform (1846-1847), hypnosis was progressively relegated to entertainment instead of clinical practice (Simpkins & Simpkins, 2002).

Nowadays, anesthesia is commonly used as synonymous with pharmacological anesthesia. Despite the undoubtful efficacy of the technique and the extreme development due to new findings in the field of pharmacology and engineering, risks and side effects can still be life-threatening in pharmacological anesthesia (Kakavouli et al., 2009; Robbertze et al., 2006; Van De Velve et al., 2009).

For this reason, "old" techniques, like hypnosis, have gained significant interest in recent years (Agard et al., 2016; Amedro et al., 2019; Berlière et al., 2018; Bonapace et al., 2018;

Ramírez Carrasco et al., 2017; Boselli et al., 2018; Claude et al., 2016; Drouet & Chedeau, 2017; Fiddaman, 2016; Fuzier et al., 2017; Hoslin et al., 2019; Jensen & Patterson, 2014; Kendrick et al., 2016; Romain et al., 2017; Sterkers et al., 2018; Waisblat et al., 2017; Zemmoura et al., 2015).

Hypnosis has been studied in several different contexts in anesthesia practice (Amedro et al., 2019; Amraoui et al., 2018; Boselli et al., 2018; Hoslin et al., 2019; Mackey, 2018), but poorly in Magnetic Resonance Imaging in pediatrics (Alexander, 2012).

With our study, in which we compared hypnosis with pharmacological anesthesia, we wanted to improve our knowledge in this specific field: the use of hypnosis in pediatric anesthesia in the context of Magnetic Resonance Imaging procedures and seek to provide information about the feasibility of this practice and its worth in this specific environment.

We use the term anesthesia as synonymous with pharmacological anesthesia in this work.

1.1. A descriptive definition of anesthesia and hypnosis

General anesthesia is a reversible pharmacologically induced depression of the Central Nervous System, determining: *loss of consciousness, amnesia, analgesia, and immobility and attenuation of autonomous responses to nociceptive stimuli* (Barash et al., 2013).

Regional anesthesia involves the reversible interruption of nerve conduction with the use of specific drugs (local anesthetics). This interruption of impulse conduction can be performed in every region of the body where the nerves are accessible to an external approach (Jankovic & Wells, 2002).

Hypnosis can be defined as the"induction of a subjective state in which alterations of perception or memory can be elicited by suggestion" (Wobst, 2007, p.1199).

These three techniques can be used separately or in combination to obtain the sufficient and necessary condition for the patient to safety undergo surgery, a diagnostic procedure, or both.

The definitions we provide on hypnosis and pharmacological anesthesia are merely descriptive and reveal nothing about the mechanisms underlying the clinical effect of both techniques.

On the other hand, the neurophysiological effects of hypnosis are the basis of its relevant impact in the anesthesiology field (Facco, 2016). Knowing something more about the mechanisms underlying the physiological effects of hypnosis and pharmacological anesthesia might be interesting to understand more deeply the phenomena and even choose the appropriate technique according to the needed neurophysiological effect. Further studies that could investigate the effect of hypnosis on specific brain areas to have the same effects of pharmacological anesthesia might be a future field of interest.

For this reason, we attempted to define pharmacological anesthesia and hypnosis functionally basing our assumptions on current scientific evidence. (SUPPLEMENTARY MATERIALS p.121)

1.2. Hypnosis and the psychophysiological variables

The albeit right limits, imposed by the scientific method, have made moving from experimental studies to routine clinical practice complicated. For example, it is challenging to distinguish measurable physiological variables that identify the hypnotic state. It is a challenge to build and reproduce a hypnotic trance reliably and to detect and register that trance in a clinical setting (Tomé-Pires & Miró, 2012).

In experimental settings, it has been possible to build hypnotic inductions with specific targets (e.g., specific pain symptoms) and verify the effects of those using, for example, functional Magnetic Resonance Imaging or Electroencephalography (EEG) or Functional Near-Infrared Spectroscopy (fNIRS) (Halsband & Wolf, 2019). Those practices cannot be readily applicable in a clinical routine, forcing to use the clinical observation of hypnosis signs to identify trance states (Erickson, 1980).

Furthermore, variables influencing the hypnotic response have also been widely investigated: the effects of hypnosis have been explained using multiple models, and none of them has absolutely prevailed among clinicians and researchers (Jensen et al., 2015).

How much biological (Faymonville et al., 2006), psychological, and social variables (Bányai, 1998; Spiegel, 2007) influence the hypnotic response has been investigated, and a biopsychosocial model of hypnosis proposed (Jensen et al., 2015). According to the aforementioned model, the following are the factors that might facilitate hypnotic responding: structural connectivity, hemisphere asymmetry, higher levels of theta bandwidth activity, expectancies, trait hypnotizability, motivation, absorptive capacity, rapport, and context.

Trait hypnotizability (Spiegel, 2007) assumes a more relevant value when hypnosis is used in surgery, but not in other procedures. Its measurement using the Hypnotic Induction Profile (HIP), which can be performed in about ten minutes, seems to be a valid tool in a context that does not allow the long times of the Stanford Hypnotic Susceptibility Scale. Regardless, in some contexts, those ten minutes might still be too much (Facco, 2016).

Meanwhile, in recent times the great interest in conscious sedation has awakened a new interest in hypnosis: hypnosedation, a combination of hypnosis with analgesic and sedative drugs. This technique easily found a place in routine practice (Faymonville et al., 1998; Faymonville et al., 2006).

This practice and the physiological variables behind the interaction of these two different tools (hypnosis and pharmacological anesthesia) open the door to new studies and clinical applications.

2. Preliminary feasibility assessment: evaluation of the clinical practice of hypnosis in anesthesia (hospital setting)

2.1. The use of hypnosis as an anesthesia technique: a historical perspective

Ether was first discovered in 1846 and chloroform in 1847, until that time traumatic procedures (e.g., Assyrians used to compress the carotid artery to induce loss of consciousness), herbs (mandragora, opium) and hypnosis were the sole forms of anesthesia. (Chidiac et al., 2012; Holzman,1998; Juvin & Desmonts, 2000; Rees, 1819; Simpkins & Simpkins, 2002; Takrouri, 1999).

Since its introduction, pharmacological anesthesia was so efficacious that the previous practices were abandoned due to a lack of interest.

Hypnosis though, nowadays, is gaining more and more interest in the field of Anesthesia (Facco, 2016), for: significantly enhanced recovery after surgery; decreased cost/benefit ratio and reduced use of drugs.

It seems that the first paper on hypnosis dates back to ancient Egypt with the Ebers papyrus (ca.1550 BC) (Simpkins & Simpkins, 2002). Hypnosis since then has been practiced in different forms.

The documented use of hypnosis as an adjunct to surgical therapy dates back to around 1830 when Jules Cloquet (1790-1883) and John Elliotson (1791-1868) performed major surgical procedures with hypnosis as a sole anesthetic agent (Hammond, 2013). Remarkable was the work of James Esdaile (1808-1859), Scottish surgeon, a pupil of Elliotson, who, when the most excellent surgeons in Europe were skeptical, traveled to India to improve his knowledge by learning from some castes that were familiar with the procedure. Esdaile performed thousands of small operations and three hundred major surgeries in India. He then obtained permission from the British Medical Association to open a mesmeric hospital in Calcutta, paving the way for the spread of hypnosis in English hospitals (Hammond, 2013; Simpkins & Simpkins 2002; Wobst, 2007).

Official medicine was slow to reintroduce hypnosis after the widespread use of pharmacological anesthesia. It was not until 1955 that the British Medical Association officially accepted to teach hypnosis at the school of medicine, and later, the American Medical

Association joined, also condemning the recreational use of hypnosis (Simpkins & Simpkins, 2002).

In order to understand the efficacy of the combination of pharmacological anesthesia with hypnosis, it is sufficient to point out that, while at the end of the nineteenth century the mortality due to anesthesia with ether and chloroform was one in four hundred anesthesias in university hospitals, in 1906 Alice Magaw reported 14.000 consecutive anesthesias without deaths at the Mayo Clinic. The way she had managed to get such a result was to use hypnosis. Hypnosis had been taught to her by her father. She induced anesthesia with drugs and continued with hypnosis (thus reducing the overall dose of the administered drugs), and reopened the ether at the end, at the wound closure (Fredericks, 2001; Magaw, 1999; De Benedittis et al., 2018).

The interest in clinical applications of hypnosis in anesthesia has been fluctuating since the end of World War II. Clinically, hypnosis has been used sporadically in a wide variety of contexts. It has been studied as a complementary technique, rather than as an alternative to anesthesia while pharmaceutical companies developed new drugs to reduce side effects and anesthesia-related mortality rates (Simpkins & Simpkins, 2012; Wobst, 2007).

2.2. Modern applications of hypnosis in the field of anesthesia

Among the many modern hypnosis applications, there seems to be an increasing interest in the following ones:

1. *Hypnosis and pharmacological anesthesia*
2. *Hypnosis in intensive care*
3. *Hypnosis in emergency conditions*

4. *Hypnosis in pain management*
5. *Hypnosis in specific populations: children*
6. *Hypnosis for anesthetic procedures outside the operating room*

2.2.1. Hypnosis and pharmacological anesthesia

In the area of pharmacological anesthesia, we can distinguish three key areas:

1) *Hypnosis as an adjuvant technique in pre-, intra- and post-operative phases in patients undergoing general anesthesia*

Pre-operative phase: Surgery is a complex stressor. Patients are affected by anticipatory anxiety; nevertheless, the subjective pre-operative factors do not receive attention and consideration in the routine management as demonstrated by the fact that the Practice Advisory for Pre-anesthesia Evaluation published by the American Society of Anesthesia does not even mention the words "anxiety" or "fear" (Facco, 2016).

Patients who are candidates for an intervention (such as those admitted to the hospital) are already in a state of altered consciousness similar to hypnosis. Therefore they are particularly responsive to the words of caregivers and, moreover, they fix the memory, due to the release of adrenaline (Weinberger et al., 1984).

The depotentiation of the conscious sets determines the suspension of critical thoughts and high suggestibility. In this condition, words, phrases, or conversations may be misinterpreted and have adverse effects (Fredericks, 2001) to the point of causing a nocebo effect, even after a poorly conducted anesthetic examination (Castelnuovo, 2013; Zech et al., 2014).

It is at this stage that pre-operative adjuvant hypnotic interventions may be appropriate. Patients who experience a low level of anxiety promptly go into a trance when talking to them as if a formal induction had just been completed, while patients in a state of high stress, although in an altered state, only hear when effective communication and vivid images capture their imagination.

Finally, it is crucial to understand the coping style of the subjects distinguishing those who prefer to be informed and those who wish to have as little information as possible.

A possible intervention in the case of traumatizing previous hospital experiences is, for example, the reframing technique (Fredericks, 2001).

The information underlined by the analysis of these pre-operative studies allowed us to define the critical issues at the moment of the induction in the hospital setting and how to utilize them in an Ericksonian approach.

Intra-operative phase: Studies have shown how patients perceive and code important information even when they are in deep anesthesia (Biescas Prat et al., 2000; Nilsson et al., 2001). Surgical anesthesia seems to block verbal, declarative, conscious memory. Words can be perceived and cause an unconscious response without conscious awareness. It is possible to recall important intra-operative events using hypnosis after surgery. However, Dawson et al. 2001 demonstrated in a double-blind study of 140 patients who underwent hysterectomy that intra-operative positive suggestions do not affect reducing post-operative pain or nausea. The use of these techniques intra-operatively has more value in investigating implicit memories than in having significant therapeutic effects.

In a meta-analysis about the use of hypnosis to manage distress related to medical procedures, Schnur et al. (2008) showed that the most effective techniques tended to be linked to a hypnotist's guidance rather than the result of recordings. On the other hand, the technique administered by the hypnotist was tented to be labeled as “hypnosis,” while the recordings, given during the medical procedure, were labeled most likely as suggestions. It was not possible to dissociate those two parameters (label and hypnosis delivery method), making it impossible to reach a definitive response about the highest efficacy of the hypnotist guidance.

Despite these limitations, Schnur et al. (2008) show the positive effects of hypnosis on perioperative emotional distress, physiological parameters, surgery duration, and outcome.

Post-operative phase: Very stressed patients experience high levels of pain intensity; they need sedatives, are more prone to infections, and are exposed to delay in the surgical wound closure.

Self-hypnosis have shown a reduction in postoperative delirium, time spent in intensive care, time of intubation, length of hospitalization, postoperative vomiting, and the need for catheterization. More early discharge from the hospital and fewer drugs, shorter convalescence, less pain from the procedure, and anxiety in children have been reported (Liossi et al., 2006). There is also a direct relationship between specific suggestions and the effect on involuntary responses, such as blood loss during surgery, glandular and visceral responses, and the increase or decrease of gastric secretions (Hammond, 2008). It is possible to have an allergic reaction to a suggestion of local anesthesia if the subject is allergic (Guttman & Ball, 2013).

2) *As an adjuvant to local anesthesia, sedation or both.*

The application methods are similar to those described for the use of hypnosis under general anesthesia, except for the induction method since patients are less likely to be in a modified state of consciousness as before a major intervention. Therefore it must be distinguished when they are in a modified state of consciousness and when they are not, to choose the induction method accordingly.

Furthermore, it is always an advantage to be able to see the patient before the operation, but the work timetable does not allow it except rarely (Hernandez & Tatarunis, 2000).

It is crucial to consider the noise present in operating theatres during inductions and pay close attention to the words used because patients can consider them literally.

Lang et al. (2006) carried out a prospective randomized trial of 236 women undergoing breast biopsies. The experiment included three interventions and relative groups: the standard treatment, empathy, and hypnosis. In the first group (Standard treatment) patients were reassured, the operators warned them of the stimuli that they were going to receive and in general received sympathy. In the second group (Empathy), the behavior was standardized (Lang et al., 1999). These were the standardized actions of the investigators: 1) imitating the verbal and non-verbal patterns of the patient, 2) listening carefully, 3) giving perception of control ("Let us know in every moment what we can do for you"), 4) responding quickly to patient requirements, 5) encouraging the patient, 6) avoiding negative suggestions ("you will receive a small puncture"), 7) using, on the contrary, neutral descriptors ("we will inject the local anesthetic "). In the third group (Hypnosis) to the latter behaviors, a standardized hypnotic induction script was added. At the end of the study, hypnosis was the most effective treatment, both in controlling pain, which increases during the procedure and for anxiety control.

Furthermore Lang et al. (2006) analyzed the limits of their study carefully: in particular, the authors underlined the impossibility of delivering a blind type of intervention, and the difficulty of making a tailoring on the patient (personalized hypnotic induction), much more effective but difficult to implement for the need to find highly specialized personnel in hypnosis and for the difficulty of reconciling the tailoring with a highly reproducible approach which is requested by a prospective randomized clinical.

In the context of the use of hypnosis in association with topical anesthesia, the prospective study by Agard et al. (2016) was carried out in 171 patients undergoing cataract surgery in hypnosis.

Preliminary results were very favorable for both patients and anesthesiologists and surgeons. The study led to an expansion of the university staff preparation program to reduce premedication in older patients and improve the quality of care.

While Amraoui et al. (2018) compared the use of hypnosis in general anesthesia for breast surgery with the traditional approach, Berlière et al. (2018) carried out a non-randomized observational study between 2010 and 2015 comparing the use of general anesthesia with sedation and local anesthesia accompanied by hypnosis always in breast surgery. The researchers hypothesized that hypnosis was able to reduce the side effects of the surgical procedure, as well as subsequent therapies and results, were in favor of the hypnosis group.

The combination of the use of sedative drugs without reaching the depth of general anesthesia and hypnosis takes the name of hypnosedation and reduces the risks associated with general anesthesia in specific patient populations and for specific interventions (Meurisse et al., 1999; Morris et al., 1985). Widely used, for example, in thyroid surgery after the first pioneering interventions of Faymonville, it continues to be published to validate its use in order to reduce the possible complications in patients with a high anesthetic risk in this type of intervention (Al-Nasser & Loucas-Gourdet 2018).

Hypnosedation is relevant when the use of certain drugs might cause danger to the patient, as in the case of Antonelli et al. (2014): they used hypnosis to perform a maxillofacial surgery with a 35-year-old polyallergic patient.

3) *As anesthetic only, in minor surgery or invasive maneuvers and selected patients or both.*

Currently, hypnosis without chemical anesthesia is rarely used; for example, when an allergy to anesthetic drugs is present (Facco et al., 2013).

Only about 10-20% of the population is thought to reach the degree of depth needed to perform major surgery. However, the advantages, in some cases, are still considerable.

In Neurosurgery, for example, where it may be necessary to check the patient's status in real-time, for example in the deep electrodes' implant (Deep Brain Stimulation) (Malafronte et al., 2016), or in gliomas' surgery (Zemmoura et al., 2016).

According to Fredericks, it is of fundamental importance that the anesthesiologist is in charge of hypnosis or in charge of all other responsibilities: monitoring vital signs or being ready to proceed with local or general anesthesia in case of need. However, in the literature, there are cases of anesthesiologists who take responsibility for both. Fredericks also suggests using hypnosis as an anesthetic with those patients who can dissociate and create positive and negative hallucinations, being the last skills, prerequisites for developing analgesia and anesthesia. When hypnosis is used as an anesthetic only it is considered a treatment in itself.

2.2.2. Hypnosis in intensive care

The state of consciousness of patients in intensive care (ICU) can vary significantly: from a state of wakefulness and complete responsiveness to pharmacologically or pathology induced coma. Patients can be hospitalized in ICU after surgery, coming from the territory or other hospitals or wards because of relevant pathologies that require intensive treatment.

It is, therefore, a heterogeneous population that will benefit from the effects of hypnosis according to the underlying pathological condition. In principle, post-operative patients will respond to treatment as if they were proceeding according to expectations if informed in advance about the admission to ICU or any necessary procedure or treatment. If they practice self-hypnosis, they will benefit from post-operative pain control.

In intensive care, the patients will present different pathologies and, consequently, different life expectancies. Fredericks (2001) suggests two techniques: the safe place and the progression to the future in relation to the underlying condition of the patient himself.

Reports suggest that patients in a coma for pathological causes (e.g., cerebrovascular pathologies) can be susceptible to suggestions (Johnson, 1987; Vanhaudenhuyse et al., 2015).

2.2.3. Hypnosis in emergency conditions

In the emergency room, in emergency conditions, the resulting changed state of conscience makes patients particularly vulnerable to the words of those who hold positions of authority (doctors, nurses). We observe literality in the understanding of the operators' statements and particular sensitivity to the non-verbal attitude of hesitation or anxiety of the staff. Identifying the signs that indicate the state of trance and giving suggestions for healing, analgesia, and reassurance according to each one's specific competence and commitment can mobilize the patients' inner resources. Particular attention should be paid to what is communicated nonverbally, including the tone of the voice.

Interesting is the effect of hypnosis on patients suffering from burns, as it can prevent the progression of lesions from lower to upper level through suggestions of cold that can influence the reaction of the tissue to the stimulus. In general, if patients respond, there is less edema, less inflammation, and less fluid loss (Ewin, 1986).

Hypnotic techniques have a noticeable effect on pain control, and in reducing anxiety in adults with burns (Provençal et al., 2018), while in children hypnosis decreases pre-procedural anxiety, but not pain intensity and does not have an effect in accelerating wound healing (Chester et al., 2018).

Patients' psychological condition in an emergency makes them susceptible to short direct and indirect inductions, and hypnosis can be used with success symptom-oriented. (Iserson, 2014; Peebles-Kleiger, 2000)

2.2.4. Hypnosis in pain management

Pain management is related to the anesthesia field. It can be considered a discipline per se or part of the clinical practice of anesthesia.

According to the applied measurement system, chronic pain affects 20 to 40% of the entire population, with different reported prevalence rates (Jensen et al., 2014). Pharmacological treatment is the most extensively used and causes high expenses for the healthcare system. However, because the experience of all types of pain is, in the end, the result of how the brain process the stimuli, many neuromodulatory therapies have been proposed as a pain treatment. Hypnosis is among them. It seems to be valid with different degrees according to the type of pain (response of 33-47% in patients with multiple sclerosis and 60% for amputation related pain), but poorly with the patient's hypnotizability (Jensen et al., 2014). Hypnosis seems to act on all the brain areas involved in pain; different words and suggestions stimulate different areas. For example, suggestions of alteration of perception act on the cingulate cortex (part of the Limbic System), and do nothing on the cortical areas involved in pain intensity. On the other hand, suggestions about pain intensity do nothing on the cingulate cortex. Furthermore, suggestions that act on the reduction of pain determine a reduction in cortical connectivity, the "pain matrix," while focusing on pleasant memories enhance cortical connectivity, "pleasure" or "comfort" matrix (Jensen et al., 2014).

To understand who is right, if those that consider the hypnosis induction process necessary to develop the neurophysiological pattern able to control pain or those that consider the induction not necessary, it is crucial to consider the physiological brain activity related to high and low hypnotizable subjects. Highs have higher baseline levels of Theta activity (relatively slow oscillations of 4-7 Herz), the opposite for the lows. Theta activity is involved in many processes: including focused and sustained concentration, reduced anxiety, and sympathetic autonomic nervous system activity, and enhanced memory functions. The fact that Theta oscillations are variably expressed in the population can explain how it is possible that different people respond in different ways to suggestions, in some cases can be seen as habitual responses, in others as something that differs from day-to-day experiences (Jensen et al., 2015).

The acknowledgment of neuromodulation's efficacy in the adult population has led to further investigations on younger patients. Even more challenging is the chronic pain treatment of young people: a worldwide and complicated endeavor. The most common pediatric pain problems are headaches, abdominal pain, and musculoskeletal pain (Miró et al., 2016).

Miró et al. (2016) reviewed the current literature about neuromodulatory treatments in pediatric chronic pain, focusing on neurofeedback, meditation, and hypnosis. In pain management, a typical hypnotic protocol can include suggestions for comfort or for coping with pain using direct instructions, metaphors, general comfort images, or specific suggestions. Treatments often include post-hypnotic suggestions to extend therapeutic benefits into the patients' daily lives (Miró et al., 2016). Self-hypnosis might be considered a first-line approach to treat chronic pain (Jensen et al., 2014).

For chronic non-cancer-related pain studies, conducted on children with headaches or functional abdominal pain, the results are overall positive even though presented in uncontrolled case series studies. Hypnosis treatment efficacy also appears to vary according to the pain condition studied.

Research demonstrated hypnosis's efficacy as a treatment for youth with chronic abdominal pain, whereas its use in the management of headaches only has modest support. (Tomé-Pires & Miró, 2012).

There is a general belief that treatment should be tailored to the patient's age for best results, but those results vary, ranging for children from 67% to 96% in the reported studies (Tomé-Pires et al., 2016).

Hypnotizability is another issue. While the association between measures of hypnotizability and hypnosis treatment in adults tends to be positive, the strength of those associations tends to be weak (Jensen et al., 2015). Regardless, high levels of trait hypnotizability do not appear to be necessary to obtain benefits from hypnotic treatments (Miró et al., 2016).

Hypnosis is also useful as a pain-control technique when used with children suffering from cancer procedure-related pain. According to the review of Tomé-Pires & Jordi Miró (2012), hypnotic interventions are significantly more effective at reducing pain than no treatment.

In summary, as underlined by Jensen et al. (2014):

· Moderate evidence supports short-term and long-term efficacy.

· Hypnosis encourages self-management and self-efficacy.

· It causes few (if any) adverse side effects and numerous beneficial side effects (for example, increased global well-being).

· Evidence supports effects on most neurophysiological processes involved in pain processing (See Supplementary material).

The outcome is variable: not everyone benefits; treatment requires patient involvement and motivation.

2.2.5. Hypnosis in specific populations: children

Hypnosis in pediatric anesthesia

Induction of general anesthesia can be distressing for children. Disrupted routines, unfamiliar faces, separation from family, hospital procedures, and uncertainty about anesthesia or surgery can be harrowing for patients and parents. Parental distress can also be transmitted easily.

Anesthesia induction can be inhalational or intravenous.

Inhalational anesthesia is induced with a volatile agent in air or nitrous oxide mixed with supplemental oxygen. A mask connected to a breathing circuit is the mean through which this kind of induction is performed (Dave, 2019).

Intravenous anesthesia induction is often avoided in children since many are scared of needles (Kennedy et al., 2008), but still used when the children are older or are more at risk during induction or when the premedication has been effective in reducing distress (Dave, 2019).

Children in both cases can protest and try to escape, prolonging the time of induction and distress and being at risk of emotional trauma. Preoperative anxiety has also been found to be associated with postoperative agitation and negative behaviors (Porter et al, 1999). The consequences of preoperative distress and pain may extend beyond the preoperative period (Alexander, 2012; Kennedy et al., 2008; Porter et al., 1999).

The level of a child’s anxiety depends on the age, maturity, temperament and previous experiences of anesthesia (Grunau et al., 1994). Sedative medications can alleviate preoperative anxiety, but children might refuse the drug, or the drug itself can cause dysphoria, preoperative behavioral changes and prolonged recovery times. Other disadvantages include safety concerns, costs, additional nursing staff and equipment, and delayed discharge.

Non-pharmacological methods for reducing anxiety and improving cooperation may avoid the adverse effects of preoperative sedation. The Cochrane review published in 2015 (Manyande et al., 2015) looked at the different non-pharmacological interventions. This review included just one study about hypnosis, despite its wide use in clinical settings. In that study, Calipel et al. (2005) found that fewer children were anxious in the hypnotherapy group compared with the midazolam premedication group, and, as a secondary outcome, they also found that fewer children demonstrated negative behavior postoperatively.

Among hypnotic interventions, the technique of safe place was found to be beneficial and it has been reported that children go quickly into trance before the administration of the anesthetics. Surgical staff can be instructed to touch the shoulder of the patient that displays discomfort as confort signal. (Lobe, 2006).

Furthermore another widely used technique in hypnoanesthesia in pediatrics is the Magic Glove particularly useful for hand intravenous catheters' insertions (Kohen & Olness, 2011).

The imaginary glove is put on the selected hand with suggestions "to know what is happening but not be bothered, as the glove protects the hand." This sensory focus absorbs the child's attention. The child is invited to experience sensory differences in the two hands and select the hand that feels less, and to consider those sensations 'okay.' Further changes in perception are suggested leading to the insertion of IV line without pain. The Magic Glove technique has been widely used in pediatrics for over 30 years. The early form of the magic glove, "the magic spot," was taught to physicians and dentists by David Elman, in 1950s and 60s (Kuttner, 2012). The insertion of IV lines in hypnosis has been studied recently by Fusco et al.

(2020) in an adult population and showed less pain and anxiety and more comfort in the hypnosis group compared to control.

About post-anesthesia recovery, Fortier et al. (2010) in a randomized controlled trial examined the effect of intraoperative positive therapeutic suggestions on postoperative nausea and vomiting (PONV) in children undergoing general anesthesia and otolaryngological surgery. Participants were 67 children undergoing tonsillectomy and adenoidectomy and their mothers. Children received a standardized anesthetic procedure and were randomly assigned to one of three interventions administered under general anesthesia: therapeutic suggestion, story (prosody control), or standard operating room noise. Children, parents, and healthcare personnel were blinded to group assignment. Nausea and vomiting were recorded in the post-anesthesia care unit and for the first three days at home. In this blinded controlled trial, therapeutic suggestion delivered intra-operatively did not impact children's PONV.

In relation to post-anesthesia, in the earlier mentioned trial of Calipel et al. (2005) comparing midazolam and hypnosis, researchers indicated a long term treatment impact: reduced anxiety from the 1st day after the surgery until the 7th day. Patients emerging from anesthesia can be nauseous, confused, bewildered, and very susceptible to suggestions. When primed with previous hypnotic induction, the patients can be more likely to respond to further suggestions of feeling hungry or re-entering the safe place as long as necessary.

Given the cumulative literature about the use of hypnosis, in particular in anesthesia and in pediatrics, it seems advisable that hypnosis becomes a standard in anesthesia practice, when conducted by hypnotists with a proper preparation (kuttner, 2012; Montgomery et al., 2002).

Hypnosis is also a valid procedure to reduce costs in a surgical setting (Montgomery et al., 2007).

Hypnosis in the Accident and Emergency Department in children

Success rates of over 90% have been achieved when using hypnosis for procedures including suturing and fracture reduction, abscess drainage, and foreign body removal (Goldie, 1956; Hopayian, 1984; Jameson, 1963).

Children are quickly bored with traditional inductions, so the technique of utilization pioneered by Milton Erickson is of great value (Hopayian, 1984). The clinical setting, even the negative behaviors, can be utilized to gain attention and induce the little patient. The main drawback is time. The reported time of induction varies from 15-20 minutes to 20-30 minutes maximum (Hopayian, 1984). These facts limit the use of hypnoanesthesia in a context where time is a critical factor. For this reason, when it is not possible in the available time to have the depth necessary to the procedure, the light trance obtained can be used to permit the infiltration of local anesthetic without discomfort (Goldie, 1956; Hopayian, 1984).

The use of hypnosis in emergency settings has been extensively recognized especially in pain management, pediatric procedures, surgery, burns, and certain psychiatric and obstetric presentations (Chester et al., 2018; Peebles-Kleiger, 2000).

2.2.6. Hypnosis for anesthetic procedures outside the operating room

Hypnosis has been used extensively in a surgical setting, but nowadays, its applications have gained success outside the operating room. Non operating Room Anesthesia (NORA) consists of anesthesia outside the surgical setting for several procedures (e. g. gastroscopies, bronchoscopies, radiological procedures). NORA procedures are often described as procedures where the anesthesiological risk is increased (Van De Velde et al., 2009).

Hypnosis gives the possibility to use fewer anesthetic drugs outside the operating room potentially reducing the utilized amount of drugs and decreasing the anesthesiological risk.

For example, Di Bona (1979) described the use of Nitric Oxide in combination with hypnotic induction for dental treatments, reporting both the description of the technique from the hypnotist and the hypnotized patient. The nitrous oxide produces slight disorientation creating a condition for which simple suggestions are sufficient. Besides, post-hypnotic inductions can be used at the end of the treatment to allow the patient to enter trance almost instantly on subsequent visits.

Hypnosis can also be used to perform invasive procedures such as gastroscopies. For example, Conlong & Rees (1999) in a study with 124 subjects reported that the hypnosis group had a significantly lower level of agitation, there were no significant differences with respect to the patient's induction time, nor differences in the time taken to perform gastroscopies, nor in oxygen saturation, while there was a significant difference in the comfort experienced: the sedated group was more at ease than the hypnosis group and the group subjected to local anesthesia, and there were no significant differences in the last two groups.

Finally, hypnosis effectively treats acute procedural pain. Kendrick et al. (2016) analyzed 29 randomized controlled trials (RCTs), showing that hypnosis reduces pain as effectively as other behavioral and psychological therapies. If hypnosis is performed in multiple sessions before the procedure, it achieves the highest percentage of results and is the most effective technique in small surgical procedures.

3. FOCUS: Hypnosis in a Radiology setting

The prolonged immobility of the Magnetic Resonance examinations and the restricted environment inside the machine can represent obstacles to some individuals. Sometimes these factors are compounded by anticipatory anxiety due to examination or pain due to the forced protracted posture if burdened by pathology.

The use and positive results of hypnosis in Radiology procedures in adults is widely documented (Lang et al., 2000; Lang et al., 2008; Lang et al., 2005; Lang et al., 1999; Lang et al., 2010; Schupp et al., 2005; Spiegel, 2006).

Lang et al. (2000) conducted a prospective, randomized single-center study with 241 patients undergoing percutaneous vascular and renal procedures. Patients were randomly assigned to receive intraoperative standard care, structured attention, and self-hypnotic relaxation. All had access to patient-controlled intravenous analgesia. Patients rated their pain and anxiety on 0-10 scales before, every 15 minutes during, and after the procedures. Structured attention and hypnosis were administered after standard training (Lang et al., 1999) of four health care providers (a nurse, two medical students. and a psychology graduate student). The providers' training was done anew by 24 h classroom instruction and roleplay, the study of a treatment manual and video, supervised clinical practice, and a second workshop lasting 8 hours. The results showed that procedures in the hypnosis group needed less time than procedures in the attention group. Patients in the standard group had significantly more medications than the attention group and the hypnosis group. About pain and anxiety: initially and for several 15 minute-periods treatment groups did not differ, but subsequently, after one hour, pain and anxiety were higher in the standard group, intermediate in the attention group, and lowest in the hypnosis group. The hypnosis group also showed higher hemodynamic stability and reduced cumulative dose of drugs administered. At the time of the 1-year follow-up, trainees had continued to build their skill levels through immediate positive patients' feedback.

Lang et al. (2008) tried to determine how hypnosis and empathic attention act on pain and anxiety, observing 201 patients undergoing embolization procedures and radio-frequency ablation of tumors. They randomly assigned the patients to three groups: standard care, emphatic attention, and self-hypnotic relaxation. They measured two primary outcomes: pain and anxiety assessed by the patient every 15 minutes, and secondary outcomes: medication use and adverse effects, including systolic blood pressure fluctuations, vasovagal episodes, cardiac events, and respiratory impairment. They concluded that hypnosis, including empathic attention, reduces pain, anxiety, and medication use; empathic approaches, on the other hand, led to an external focus of attention and did not enhance individuals' coping skills, resulting in significant adverse effects. These findings could have implications in structuring staff training programs. A possible explanation for the increased incidence of side effects (in particular hemodynamic effects) on patients of the Empathy group is that hypnosis reduces the sympathetic activity of the heart and the risk of myocardial ischemia during angioplasty and enhances the profile of the heart rate variability (a quantitative measure of the changes in the intervals between heartbeats associated with autonomous function and a cardiovascular risk prediction). Patients in the standard care group may be spontaneously in trance, because the trance can occur spontaneously without formal induction, especially in stressful conditions. This fact can reduce side effects in their group in a way that is similar to the hypnosis group. The Empathy group, instead stimulated continuously by the staff to talk about external topics according to the pattern of social interactions, may not only have problems implementing their coping systems, but they may also feel a lack of interest from staff.

Lang et al. (2005) analyzed the videotapes recorded on 159 patients undergoing percutaneous vascular and renal procedures that were randomly assigned to receive intraoperatively standard care treatment, structured attention, and hypnosis. The results showed that warnings and commiserations did not help reduce pain and anxiety. When communications were negatively-loaded it could become a self-fulfilling prophecy. Furthermore, the suffering associated with these communications could suggest to providers that it was appropriate to use them.

Lang et al. (2010) showed the effectiveness of staff training in improving patient compliance with Resonance procedures and how hypnosis has also been used to reduce the discomfort of interventional radiology procedures.

Schupp et al. (2005) investigated 236 patients' anxiety, need for drugs, and duration of their exams during their vascular and renal interventional procedures. They randomly assigned the patients to three interventions: standard care treatment, structured empathic attention, and self-hypnotic relaxation, and further divided those patients into two groups: those with low state anxiety scores on the State-Trait Anxiety Inventory (STAI<43) and those with low state anxiety scores (>or =43). All had access to patient-controlled analgesia. Every 15 minutes during the procedure, patients rated their anxiety and pain on a scale of 0-10 (0, no pain/anxiety at all; 10, worst possible pain/anxiety). Those receiving hypnosis showed reduced procedure time and medication use in both the high-level anxiety and low-level anxiety groups. Hypnosis was more effective than standard care to reduce pain and anxiety, and because high anxiety group patients are the ones that have higher procedural pain and anxiety, they are the ones that can benefit the most by hypnosis. More efficacious than standard care was emphatic attention too. Both the highly anxious and the low anxiety group can benefit from non-pharmacological treatments.

Spiegel (2006) underlined the mounting evidence of hypnosis's benefits in the radiology suite with adult patients. He described the use of hypnosis, an ancient technique, in a radiology setting, a modern field, as a wedding. Nevertheless, he pointed out something blue: the extended family did not come to the wedding. Reasons are complex, and Spiegel mentioned that maybe physicians are suspicious of treatments that involve talk and relationships rather than medications and nerve blocks; maybe it is because no intervening pharmaceutical industry wants to sell this product.

Children commonly require sedation to complete radiologic imaging exams or procedures: sedation is a broad name that includes various techniques, ranging from anxiolysis to general anesthesia (Boswinkel & Litman, 2014). Some children have difficulties due to their clinical condition. Some have a very young age, some express concern for the length of the exam, the noise, the intimidating size of the machine, many are frightened, sensitized by previous experiences, or by their caregivers' fears.

Prior studies on children have recognized the utility of hypnosis in order to complete painful and not painful procedures, and an analysis of all the techniques used in the radiological setting has been published (Alexander, 2012).

Butler et al. (2005) studied pediatric patients undergoing cystography in hypnosis and reported good results. They randomized 44 children into two groups: the standard care group and the hypnosis group. Parents were contacted by telephone and invited to participate if the child was eligible. Each child and parent met with the research assistant before the day of the scheduled procedure for an initial assessment and instructed about the self-hypnotic session. Parents and children were instructed to exercise with the hypnotic procedure several times a day. Results showed that children assisted by hypnosis presented less distress than those under standard treatment, and the radiologic procedures were almost 14 minutes shorter.

General anesthesia (GA) is often needed for radiotherapy (RT) in young children. Claude et al. (2016), with their observational study, retrospectively collected data on GA in children under 5 years old treated by RT in a reference center in pediatric radiation oncology between 2003 and 2014. Before and after 2008, two-time periods were compared, the second one introducing accompaniment methods such as hypnosis systematically. Explanatory analyses of GA were performed using logistic regression. The study confirmed that rituals and hypnosis could be used instead of GA in about half of patients under five years, even with high-technicity RT requiring optimal immobilization.

Several studies suggested that hypnosis has been effective in a radiologic setting in an adult population, and that training personnel was efficacious to reduce dropouts in MRI exams in adults due to anxiety (Alexander, 2012; Lang et al., 2000; Schupp et al., 2005), but little is known about children in this specific context: the efficacy of the hypnotic treatment is attempted to be proved by the use of it in interventional procedures, before anesthesia and in abdominal pain or specific populations (autism) (Edwards & Arthurs, 2011). More research is needed to investigate further the use of hypnosis in reducing stress in the radiology department in pediatrics as underlined by Alexander (2012).

In a radiology setting and especially during MRI exams, more studies in pediatric patients might be useful to prove the technique's actual efficacy. What is missing are more data that might show how this technique can be really used in such a complex environment like an MRI setting in pediatrics in a daily routine, as part of the clinical practice, overcoming the environmental challenges and what is missing more are cases of physicians that have the courage to challenge that glass ceiling underlined by Spiegel (2006).

II. OBJECTIVES AND HYPOTHESIS

OBJECTIVES AND HYPOTHESIS

Objectives

The general aim of this doctoral dissertation was to improve our knowledge on hypnosis when used with pediatric patients in the MRI setting.

Specifically, we had two objectives: first of all, we wanted to develop a protocol based on the Ericksonian hypnotic approach to manage distress and allow steadiness during MRI exams in pediatric patients. Second, we wanted to study the effects of the protocol, when used with pediatric patients undergoing MRI exams in a hospital setting (Tertiary Care Pediatric Hospital), on the following variables: drug consumption, anxiety, pain intensity, number of patients that stopped using anesthesia after the procedure hypnosis, presence of artefacts, MRI exam duration, anesthesiological risk.

Hypothesis

Given previous research findings, summarized in the previous section, we hypothesized:

a significant effect of hypnosis on reducing drug consumption (with a positive impact on reducing the anesthesiological risk) and reducing anxiety and pain intensity in the hypnosis group compared with the anesthesia group;

that hypnosis could have a long-term effect reducing the need for anesthesia in further MRI exams in the hypnosis group;

that hypnosis could increase exam duration and artefacts in the hypnosis group compared with the anesthesia group, not compromising the reliability of the exams.

III. METHODS

METHODS

1. Participants

Participants were a sample of 108 pediatric patients whose parents gave their informed consent.

1.1. Inclusion criteria

- Patients scheduled for anesthesia only because of their age (below 10 years old)

- Patients who did not have acute pain, whose pain allowed them to lay down in MRI, or both. Patients were positioned in the machine and asked in case of doubt.

- Patients who expressed fear of the MRI exam, its outcome, or both.

- Patients whose parents voiced concern about the magnetic resonance exam, its result, or both and who believed that their child was equally afraid, were unable to carry out the examination awake, or both.

- Patients that had done an MRI exam before or not.

1.2. Exclusion criteria

- Patients who suffered from any disease or under any drug treatment that could alter the state of consciousness.

- Patients with acute pain who had troubles lying in the MRI

- Patients with psychosis.

2. Procedures

2.1. Recruitment and group allocation

Parents of all children who had to undergo general anesthesia (sedation with a Laryngeal Mask Airway, LMA) to perform an MRI exam; and were eligible, according to inclusion and exclusion criteria, were offered to participate in the study.

The children in the hypnosis group were recruited at the moment of the induction of anesthesia when they and their parents expressed their consent for the hypnotic procedure.

2.2. Hypnotic procedure

Hypnosis was introduced in MRI for the first time in the history of the hospital. This clinical activity and the investigator's profile (expert in hypnosedation) were officially approved. In Italy, a medical doctor can become a psychotherapist after accomplishing a 4-year specialty course. When an anesthesiologist accomplishes the psychotherapy course, as in the case of the investigator of this Dissertation, that person is licensed to perform both anesthesia and hypnosis.

A hypnotic approach was introduced (Ericksonian psychotherapy) in the routine practice of the Radiology department of Meyer hospital (Florence, Italy), and all the children scheduled to undergo general anesthesia (sedation), that could be enrolled from January 2015 to December

2016, mostly during the shifts assigned by the department to the researcher (from January 2015 to June 2016), were treated with a hypnotic approach.

The hypnotic approach was a creative, individual patient-tailored response to the challenges encountered in this complicated and specific context; every aspect of the environment was used as part of the induction and to deepen the trance according to the principle of utilization.

After a very quick hypnotic anamnesis and the observation of ideomotor responses, the investigator performed the hypnotic induction to realize the procedure.

The hypnotic induction procedure included caregivers, toys of the child, the collaboration of the personnel, and pseudoscientific explanations (every means available), with a tailored approach.

The anesthesiologist conducted the pre-anesthesia and the pre-hypnosis assessment (with eventually the hypnotic induction) in a time frame of about 30 minutes. Furthermore, the anesthesiologist decided to use hypnosis instead of sedation after this assessment on the day of the procedure.

Despite being tailored, the approach had a consistent structure built through careful observation of the characteristics of that specific environment, the standard challenges of a NORA procedure, and those peculiar to an MRI exam in children. Here in the following paragraph details about the procedure.

2.2.1. The physical and social context of the environment

The hospital was a third-level Pediatric Hospital with complex and high-risk medical patients. The MRI setting was noisy, chaotic, and in an open space. Anesthesiologists performed anesthesia and a pre-anesthesia assessment on the spot. Children were put asleep in front of at least one parent, and after the completion of the MRI procedure, they had the parents' company for about one hour or more until full recovery. Parents and monitored children were staying in the same areas (an open space separated by tents). There were two MRI (1.5 TESLA and 3 TESLA) machines and a CT scan (located in a next-door space), all of which were under the same anesthesiologist's responsibility. Three technicians, one for each machine and two nurses (one for the MRI machines, another one for the CT scan, and the other radiological traditional procedures), were in charge in the same environment.

This description is functional for understanding the specific challenges of the environment.

Immediately outside this open space, there was a play MRI. A small MRI in which an interactive cartoon could have been useful to children to become acquainted with the procedure and the machine. This area was recently built and rarely used in the clinical routine at that time.

2.2.2. Control group

A control group homogeneous for age, sex, and type of MRI exam was selected among the department's patients treated by other colleagues. The performed anesthesia technique was very homogeneous in this particular setting and used by all colleagues (in the hospital, the anesthesia procedure in MRI is standardized). It was based on inhalation of sevoflurane, an anesthetic gas belonging to the group of halogenates, and the insertion of a laryngeal mask.

Patients were selected among those treated by the other colleagues because the investigator used Ericksonian psychotherapy in her common clinical practice as preparation before anesthesia, which could be a confounding factor.

2.2.3. Assessment

The first assessment of the children was conducted at the entrance of the MRI area while welcoming the family. It was identified as the primary caregiver through observation of the family group, and he/she was considered from that point on as the main ally in the procedure that would have followed.

Each child was addressed directly and using a 45 grades approach and at the same height, using language appropriate with his or her age.

The anesthesiologist started by presenting herself as anesthesiologist and psychotherapist to the parents, saying that she would collect the information necessary to perform anesthesia and also evaluate if the child was ready to perform MRI without sedation through an Ericksonian psychological intervention.

All parents agreed with the fact that it was preferable to avoid anesthesia, if possible. Still, very often, they had doubts regarding the capability of their child to take the exam without drugs; sometimes, the child was more confident than them. In a case, a father, after being reluctant to give trust to his son, when asked to enter the MRI during the procedure, confessed to be phobic. His son accomplished the exam without problems. The father was in the MRI room with him during the procedure.

Previous experiences with MRI were asked before any other question.

The primary goals to accomplish at the beginning of the interview were: gaining attention, building trust, and changing the locus of control. The anesthesia assessment started by asking the child to correct his/her parents if they were answering wrong about his/her personal information. This simple statement made the child feel in charge of the situation and gave him/her a sense of control. Furthermore, the anesthesiologist used to present herself as engaged in doing homework, being the latter statement a useful way to create attunement, especially with a scholarly child.

2.2.4. Interventions

Acknowledging the feeling of the child and acting in accordance was a fundamental step to build a relationship of trust. Tailoring the intervention on the child was crucial. During the process, the investigator observed the child's minimal cues and asked the child's judgment about what his/her parents' were saying. Before explaining the anesthesia procedure and its risks, once gained the child's full attention, the MRI procedure was described as a machine taking a picture, an extraordinary picture of the inside, to raise the child's curiosity. The investigator described the gate according to the interests of the child; interests explored with the parents when possible. The machine had the shape of an animal net, a space shuttle, or else. The investigator described it in different ways (using metaphors) and looking for the child's response of approval (verbal or non-verbal). Once individualized, the metaphor that caught the child's attention was implemented using a language that could stimulate different sensory channels. The investigator suggested that in the gate, it was not necessary to keep awake all the time. The patient could sleep and go to a pleasant and comfortable place, the one he/she found previously talking with the investigator (the space shuttle or the net) or any other of his/her choice.

The investigator asked the child about his/her favorite place. The place was co-constructed with him/her through the different sensory channels, having more details from the child about it and starting observing his/her absorption in the description.

During the description, the investigator and child used the present tense.

The investigator suggested a distortion of time perception, reminding him/her how time flies when we do something we like (and why not doing it in that pleasant place?).

The investigator made the child explore that distortion with different examples, giving him/her the illusion of choice among different possible subjective perceptions of the length of the exam, showing curiosity about how fast the time would be in the child's safe place.

If possible (if there were no technical contraindications: the presence of not compatible metal implanted devices, pacemakers, pregnancy, for example), the primary caregiver followed the child in the MRI.

The investigator suggested to the parent to touch the child, if possible.

If it was not possible because the parent had to enter too deeply into the gate and that was not allowed for safety reasons, the investigator instructed the parent to look at the child through a specific mirror present on the helmet of the MRI.

Sometimes the investigator started a competition between the child and the parent, betting on who was more still. Other times the investigator asked the child if he or she preferred to bring the parent into his/her favorite place.

According to his/her individuality, the child had the option to be in competition or cooperate with the parent.

The investigator introduced a new idea in the MRI hypnotic treatment: she prescribed the "symptom" movement. This prescription was very efficacious to have the patient still for such a long time. The child was asked to move whenever he wanted a hand or a foot according to the MRI exam: for example, if the patient had to do an MRI scan of the head, he or she could move the favorite hand. It was always given an illusion of choice, and whenever the patient wanted to move, he/she could choose between at least two possible options.

To keep the patient still and in hypnosis for the entire procedure, the investigator utilized the noise, considering it positive and not scary or a distraction. The noise of MRI is peculiar: it is impulsive and is felt inside as a shake, especially in MRI 3 TESLA. So it was said to the child that whenever he or she had listened to the noise or felt it, he/she would have gone more deeply into sleep or would have gone back to his/her favorite place. In case the child could be touched by the parent, then was the touch of the parent that would have brought him/her deeply, or seeing the parent (he or she were used as anchors too), or feeling the machine under or around him. These commands had the scope to keep the trance deep for the entire exam.

Always during the explanation, the investigator told the child that once called at the end of the exam, he or she would feel fully awaken, relaxed, happy, and curious about what he/she had done in this favorite place and would feel hungry and ready to eat something he or she liked. It was also added a post-hypnotic command that he/she would have been ready to use what learned whenever needed.

Some children had to introduce a vein catheter to inject contrast medium. In this specific case, the patient was asked to inform which hand was feeling less, then was asked to which extent (touching the hand) was feeling less and were introduced metaphors of cold and sleeping hands talking about the snow (as well as cold things) and how it could make hands cold and sleepy and maybe a little tickling.

Before deciding if he/she could or could not perform the MRI exam, the child was brought in front of the machine MRI. In front of the screens, he/she could see a few seconds images of inside the body and the machine behind the glass. At this point, it was asked directly to the child if he thought he could do it, and by observing not only the answer but the non-verbal communication of the child, it was possible to understand if the patient was capable of doing it or "needed more time," to use the words that were used to explain to him/her.

Once the child was conducted inside the MRI room, the explanation of the different parts of the MRI continued. A little bell was shown to the patient. It was explained to the child that he/she could ring if he/she had something significant to ask, knowing that if he/she used it and could not wait until the end of the exam, the MRI procedure would have lasted longer. No mention was made of problems or used words that could resemble any trouble with the machine. The patient was reassured that the parent would have stayed inside the MRI room, watching over him, and if not possible, the staff would have taken care of him/her, watching through the window all the time. When the child had to wear the helmet or enter the gate, all was done in a calm and not stressed explanation, a gentle flux of air was made him notice coming through the gate, and a moment before entering the gate, it was asked if he was already in that beautiful place and if we could enter the gate. After an affirmative answer, the child would be moved into the machine. At this stage, it was possible to notice a slower trancelike, no verbal answer.

In all the stages, especially in preschooler children, were used transitional objects inside and outside the MRI, in preschoolers was also very useful to start the conversation by pretending to be something and building on it the suggestions of hypnosis: like the kid that thought to be a tree and slightly moved in the MRI because there was the wind.

All the explanations were made in front of the personnel involving them, but at that time, the personnel was stressed and so was not accepting "waste of time," some being significantly in opposition with any technique apart from anesthesia. Despite that, it was possible to train them and explain to them all the main principles of Ericksonian psychotherapy and the techniques used in MRI. It was possible to teach them to reduce the nocebo effects of misplaced words (for example: "when you enter the gate, you will feel a lack of air, "said one of the technicians at that time with, of course, predictable results).

2.2.5. Environment management

The personnel's nocebo effects were challenging to handle, so it was introduced into all the inductions to ignore other disturbing voices that the patient did not like. The latter was necessary considering not only the noise but also the negative messages from the personnel.

The researcher conducted a four-hour seminar to inform the personnel about the hypnotic procedures and increase their communication skills in order to reduce, when possible, the nocebo effect and possibly use their new abilities to reduce the need for anesthesia. After completing the seminar, personnel absorbed the principles but still kept in opposition to the procedure due to the lack of time and extreme intense rhythm of work.

For that reason, in the last six months of 2016, on Saturday morning, it was decided to use the room of the play MRI for the preparation of patients. In this way, the inductions and explanations to patients were held in a more quiet place, but the procedure was the same.

As part of the play MRI, there were reproductions of devices (bell, headphones) that helped to introduce the parts of MRI that the child would find at the exam and using the pets that were there for the explanations (pets were used sometimes also as an explanation of the procedure of induction of anesthesia). In the beginning, the parents did not want to come an extra day to be prepared for the exam, have the option to come the same day of the exam, and try the MRI awaken, but their compliance improved when it was decided not to do so.

So the Saturday morning, the play MRI room was put at disposition for those interested and called those who could be enrolled.

2.2.6. Environment nocebo effect: strategies to develop a consistent change

As already mentioned above:

1. Negative suggestions function as priming. Words that refer to unpleasant experiences are registered literally and influence patients' responses, suggesting specific symptoms. Those mistakes are made with no intention of harm nor awareness (Lang et al. 2005).

2. Personnel training proved efficacious in reducing drop-outs in adults in MRI (Lang et al., 2010).

In order to

A. minimize nocebo effect,

B. give information about the hypnotic procedure employed in the MRI,

C. train personnel in Ericksonian communication to improve the quality of care and, as a consequence, reduce the overall anesthesia rate, the investigator conducted a course. The meetings were repeated six times during 2015 to allow all nurses and technicians of the radiology department to attend without interrupting the clinical practice.

Two meetings made each course:

In the first meeting, the investigator explained the general principles of Ericksonian hypnosis; in the second meeting, she described the specific procedure used in MRI, and a group induction was performed following the script used by Lang in the MRI (Lang et al., 1999).

After each course, the participants answered a questionnaire in which was assessed:

1. The relevance of the topic

2. Educational quality

3. Utility

4. Quality of the organization

5. Teaching quality

6. Suggestions and comments

Eleven people took part in the courses voluntarily: three nurses and eight technicians. It was possible to work with each person individually.

The experience was shared with medical staff at the end of the year in a Risk Management meeting, underling the utility to train personnel to improve their communication skills.

Measures:

To measure items 1 to 4, we used 0 to 5 scales. Averages were:

1. The relevance of the topic: 3.8

2. Educational quality: 4

3. Utility: 3.6

4. Quality of organization:3.8

The fifth item *5. Teaching quality* was comprehensive of other three sub-items:

1. Clarity of expression and knowledge of topics: average 4.4

2. Capacity to interact with participants: average 3.8

3. Time management and didactic supports: average 4.2

The sixth item *6. Suggestions and comments* comprehended all requests for more lessons to deepen the knowledge in this field, focusing on the Radiology department and non-verbal communication.

A stressful environment might be responsible for a less caring attitude towards patients (Lang et al., 2010). As shown in Table 1, the number of MRI exams increased dramatically in 2015 and 2016, leading to the dismissal of any technique that was not proved to be extremely productive (number of patients' exams/time). As mentioned above, it was then decided to organize any preparation of patients in the MRI simulator on Saturday morning (June-December 2016).

Table 1: NUMBER OF MRI EXAMS FROM 2014 TO 2019 (SEPTEMBER)

TABLE 1					
2014	**2015**	**2016**	**2017**	**2018**	**2019 (September)**
8.101	9.466	10.882	11.175	10.779	7.670

The introduction of communication skills based on Ericksonian psychotherapy among personnel changed the hospital's choice to plan for all children until ten years old MRI exams in anesthesia. Instead, all children above eight started taking MRI exams awaken after a family Saturday meeting in the MRI simulator.

3. Measures

Drug consumption. We performed an analysis of the drugs used in both procedures, showing the average use of medications in MRI per patient.

Anxiety. We used a Verbal Anxiety Rating Scale (VARS), ranging from 0 "no anxiety" to 10 "feeling of being terrified" before and after the procedure hypnosis. Participants were requested to report the number that best reflected the level of anxiety that they were experiencing. The VARS has been shown to provide valid and reliable anxiety scores when used with this population (Benotsch et al., 2000).

Pain intensity. Children reported their pain intensity on a Numerical Rating Scale (NRS-11) scale from 0 (no pain) to 10 (very much pain). NRS-11 has demonstrated excellent psychometric properties when used with children as young as 6 years old (Castarlenas et al., 2017). Patients show good compliance because it is a score easy to administer if compared with other self-report tests (Castarlenas et al., 2016).

When the child could not report the number correspondent to his/her pain intensity, we asked parents. Using parents or health care professionals (e.g., nurses) to report pain when a patient cannot directly inform about this is common practice. For example, Labajo et al. (2017) showed that agreement between parents and children was excellent for the highest pain intensity domain.

Measures of pain intensity (using a Numerical Rating Scale scale from 0 to 10) were performed when suitable with the exam (introduction of peripheral venous catheters) before and after the procedure hypnosis and when the patient experienced pain due to his/her disease.

Presence of artefacts.

In order to analyze the correlation of hypnosis with the presence of artefacts, we checked all the reports of the MRI exams and measured:

1. The number of exams with artefacts in the hypnosis group.

2. The presence of artefacts in exams realized in the MRI 3 TESLA machine in the hypnosis group.

In MRI, all that is represented in the image without correlation with the real anatomy or functional map of the information sought in the examined layer can be defined as an artefact (Coriasco, 2014).

Different reasons can cause artefacts in MRI exams. We analyzed the presence of images with artefacts due to the movement of the patient, specifically those artefacts referred to the body area checked in the exam. In MRI, the study of a district is carried out through an overall evaluation of multiple images obtained in various sequences. Each time the patient moves, generating artefacts, the radiologist stops the exam, and the acquisition of images lasts much longer because it is necessary to repeat the entire sequence from the beginning. Each sequence of images represents a different way of displaying that anatomical portion and provides information on the nature of the tissues (healthy or pathological) present in it.

TESLA is a measure of the magnetic field density ("IUPAC Compend. Chem. Terminol.," 2009). 3 TESLA MRI is an MRI machine with a magnetic field of 3 TESLA. It is a more intense field (doubled) than 1.5 TESLA, and this intensity determines more noise; this noise is also felt as an impulse that shakes the patient's body in the machine. 3 TESLA MRI machine impulse is generally referred to as more disturbing by patients.

Wardlaw et al. (2012) systematically reviewed studies comparing diagnostic accuracy at 3 T with 1.5 T. They analyzed 150 studies (4500 subjects); most were tiny, which compared 1,5 T with new 3 T technology. The 3T images were described as "crisper," but they found little evidence of an improved diagnosis; improvements were limited to specific applications (e.g., fMRI, spectroscopy). Artefacts were worse, and acquisitions took slightly longer.

The choice of correlating the presence of artefacts with the field of the MRI machine (1.5 and 3 TESLA) is due to the higher sensitivity and intensity of noise of 3 TESLA MRI. We hypothesized as more challenging to accomplish the exam in 3 TESLA than 1.5 TESLA MRI and wanted to verify if this hypothesis would have been significant in the group hypnosis influencing the correlation between artefacts and hypnosis.

3. Presence of artefacts in patients' exams that introduced a vein catheter to inject MRI contrast agent (Gadolinium (Gd), a rare-earth metal with paramagnetic properties) in the hypnosis group.

For some MRI exams, it is necessary to use a contrast medium, a substance used to increase the contrast of specific structures that have to be investigated (e.g., tumors). Introducing a vein catheter can be distressing for patients.

The choice of correlating the presence of artefacts with the vein catheter positioning was due to stress that every child experiences at the positioning of the vein catheter. We wanted to check if the positioning could affect the accomplishment of the MRI exam causing more artefacts and influence the correlation between artefacts and hypnosis.

We also reported if there were repeated exams because not diagnostic and missed sequences of images.

Patients that stopped using anesthesia for MRI after the exam in hypnosis.

In order to analyze the difference in the behavior of children after the procedure hypnosis, we measured:

1. Number of patients in both groups that performed MRI exams awaken after the procedure examined (hypnosis vs. anesthesia),

2. Number of patients in the hypnosis group that performed MRI exams awake after the procedure and before needed anesthesia for MRI exams.

MRI exam duration.

We compared the length in minutes of all the MRI exams between the hypnosis and anesthesia groups.

For the sake of brevity and clarity, we summarize the variables and measures used in the study in Table 2.

Table 2. Variables and measures used in the study

Variables	**Measures**
Drug consumption	Amount per patient
Anxiety	Numerical Rating Scale (0-10)
Pain intensity	Numerical Rating Scale (0-10)
Artefacts	Number /%
Artefacts vs. 3 TESLA	Number/%

Artefacts vs. Vein	Number/%
Awaken after procedure	Number of patients that stopped using anesthesia for MRI
Awaken after hypnosis and under anesthesia before	Number of patients that stopped using anesthesia for MRI and were put under anesthesia before
MRI exam duration	Minutes
Anesthesiological risk	Number

3.1. Data analysis

In this transversal observational study, we studied a group of patients who received the treatment hypnosis during routine practice for MRI exams and compared the results of the variables analyzed with a group of patients who received anesthesia in the same environment with the same type of exams.

Data were extracted from various databases and matched with Meyer hospital Department Physics' support and analyzed with the collaboration of University of Campania "Luigi Vanvitelli."

Exploratory Data Analysis (EDA) was done in order to clarify their general form to check for discrepant or extreme observation, producing numerical summaries of the data.

Definitive Analysis included both descriptive and analytical inference performed with Excel and Matlab.

To demonstrate the statistical independence for sex, age, type of exam performed in MRI, duration of the examination, presence of artefacts, the magnetic field strength, and exams with medium contrast between hypnosis group and anesthesia group, we used Fisher's exact test. We used separation criteria to emphasize the population's differences (medians 8 years for the age, and 40 minutes for the examination duration). If $p < 0.05$, the observed differences cannot be attributed to chance alone.

To confront the hypnosis group and the anesthesia group, we also used the U-Mann-Whitney test for continuous variables (age, duration of examination). A p-value inferior to 0.05 was considered statistically significant. The continuous variables were summarized with median and standard deviation if normally distributed and with interquartile range (IQR) if not normally distributed.

For pain and anxiety, the Wilcoxon test has been used. The two-sided Wilcoxon rank-sum test can test the null hypothesis that data in the two groups are samples from continuous distributions with equal medians, against the alternative that they are not. The Wilcoxon test is non-parametric and ignores the normality of the distribution.

In order to measure if patients stopped using anesthesia for MRI after the exam in hypnosis, Odds ratio test has been used. The Odds ratio is indicated when we want to test the efficacy of a factor to change the outcome. In this specific case, the Odds ratio was used to measure if the hypnosis procedure was efficacious to change children's behavioral patterns, making them more likely to accomplish the MRI exams without anesthesia.

IV. RESULTS

RESULTS

1. Sample characteristics

A total of 108 patients from 3 to 19 years old participated in this hypnosis study. All patients were tertiary care patients from Meyer Children's hospital, Florence (Italy), who had to undergo MRI exams, both inpatients and outpatients. All patients enrolled in the group hypnosis were scheduled for sedation during MRI. It means that all were planned to be performed under anesthesia.

Fifty-eight were enrolled in the hypnosis group and fifty in the anesthesia group. Of the 58 participants that were planned to receive hypnosis as a treatment: 27 were female, and 31 were male. N=56 patients succeeded; two patients were enrolled but did not accomplish the exam: one for his referring physician opposition, the other for agitation. The patients that could not make the exam were respectively: 6 and 8 years old, both males. Patients enrolled in the two groups were similar for sex, age, and MRI exam performed. After the procedure, the participants were debriefed.

We demonstrated the statistical independence for sex, age, type of MRI exam performed, duration of the examination, presence of artefacts, the magnetic field strength, and exams with contrast medium between hypnosis group and anesthesia group.

Tables 3,4, and 5 show descriptive information about the study sample.

TABLE 3: Patients' demographics: sex, age.

Parameters of 56 participants in the hypnosis group and 50 participants in the anesthesia group enrolled in the hypnosis study in the Department of Radiology, in AOU Meyer 2015-2019

Variables		**Hypnosis group**		**Anesthesia group**	
		N	%	N	%
Sex	Male	29	(52)	27	(54)
	Female	27	(48)	23	(46)

Fisher's exact test:

p=0.82

P<0.05 is significant

Age of 56 patients treated with hypnosis	**Hypnosis group**	**Anesthesia group**
Mean	8,4	8.6
SD	3	3.1
Median	7.5	8.5
Min	3	3
Max	19	19

Mann-Whitney U test:

p=0.66

P<0.05 is significant

TABLE 4: Patients' demographics: exam's duration in minutes, artefacts reported by radiologist clinical report, MRI magnetic field strength (1.5 and 3 Tesla), use of contrast medium for the specific exam (contrast medium)

Parameters of 56 participants in the hypnosis group and 50 participants in the anesthesia group enrolled in the hypnosis study in the Department of Radiology, in AOU Meyer 2015-2019

Variable		**Hypnosis group**		**Anesthesia group**	
		N	%	N	%
Minutes of the exam	<40	22	(39.3)	24	(48.0)
	≥40	34	(60.7)	26	(52.0)

Fisher's exact test:

p = 0.43

Note: We used a separation criteria (median 40 min) to emphasize the population's differences.

Artefacts	No	48	(86)	50	(100)
	Yes	8	(14)	0	(-)

Fisher's exact test: p=0.005

Tesla	**1.5**	34	(61)	25	(50)
	3	22	(39)	25	(50)

Fisher's exact test: p=0.27

Contrast Medium	No	34	(61)	22	(44)
	Yes	22	(39)	28	(56)

Fisher's exact test:

p=0.085

Variable	Hypnosis group	Anesthesia group
Minutes of the exam		
Mean	44.68	43.0
IQR	33.5, 53.5	35, 52
Median	43.0	40.0
Min	25.0	17.0
Max	82.0	88.0

Anesthesia group and hypnosis group were homogenous for the type of exam in MRI performed. Table 5 shows subcategories of the exams performed. We chose to organize the exams in subgroups according to the specific challenges we could encounter during the hypnosis procedure in each body area.

TABLE 5: Patients' demographics.

Parameters of 56 participants in the hypnosis group and 50 participants in the anesthesia group enrolled in the hypnosis study in the Department of Radiology, in AOU Meyer 2015-2019. Sub-categories of the body areas investigated in the study group **(hypnosis group and anesthesia group)**

Hypnosis group-Anesthesia group	Sub-categories	Number
Hypnosis group	Head-neck	43
	Column	4
	Thorac-Abdomen	3
	Limbs	6
Anesthesia group	Head-neck	39
	Limbs	2
	Column	6
	Thorac-Abdomen	3
Fisher's exact test: **p = 0.38**		

2. Results for each variable measured

2.1 *Drug consumption.* About drug consumption we performed an analysis of the drugs used in both procedures. Due to the impossibility to identify for each patient the amount of drugs used, we considered the official data of the average use of drugs in MRI per patient in Meyer hospital, Florence.

The following is the calculation based on the annual number of cases. In particular it was realized considering the year 2018 and the analysis was performed on 2800 patients that received anesthesia during MRI procedures. Conclusion of the analysis, whose details have not been made public, were that: a bottle of Sevorane 250 ml is used every five patients, considering the mean age of patients 7 years old, the mean weight 25 Kg, the duration of anesthesia with 3.5 MAC (MAC= Minimum Alveolar Concentration: the concentration of a vapor in the alveoli of the lungs that is needed to prevent movement (motor response) in 50% of subjects in response to surgical (pain) stimulus) of 60 minutes.

Furthermore, every day in the MRI area of Meyer hospital, an ampulla of Midazolam 5 mg and a bottle of propofol 100 mg are available, but the consumption is marginal.

The latter can be considered as the drug consumption in the anesthesia group; in the hypnosis group, on the other hand, two patients received drugs: one that received hypnosedation and was injected intravenously with midazolam 3mg, and one that used nitrous oxide for vein catheter introduction.

2.2. Anxiety. We used a Verbal Anxiety Rating Scale (VARS), ranging from 0 “ no anxiety” to 10 “feeling of being terrified”, before and after the procedure hypnosis in the hypnosis group. We found that anxiety was significantly reduced in the hypnosis group after the procedure **(**P.VALUE (WILCOXON TEST) <0.001)

We summarize the results in the following table:

TABLE 6: Anxiety in hypnosis group. Measure of anxiety in the hypnosis group with the scale VARS (0-10).The label "anxiety_pre" indicates the measure VARS (0-10) before the hypnosis procedure and "anxiety_post" indicates the measure VARS (0-10) after the hypnosis procedure in each patient of the hypnosis group.

	"ANXIETY_PRE"	VS.	"ANXIETY_POST"
MEDIAN	6		0
RANGE	(0-10)		(0-10)

P.VALUE (WILCOXON TEST) <0.001

P<0.05 is significant

2.3 Pain intensity. Measures of pain intensity (using a Numerical Rating Scale scale from 0 to 10) were performed when suitable with the exam (introduction of peripheral venous catheters), and when the patient experienced pain due to his/her disease before and after the procedure MRI in hypnosis. Pain intensity was not significantly different in the hypnosis group before and after the procedure (P.VALUE (WILCOXON TEST) =0.097).

TABLE 7: Pain intensity in hypnosis group. Measures of pain intensity (using a Numerical Rating Scale scale from 0 to 10). The label "PAIN_PRE" indicates the measure NRS (0-10) before the MRI in hypnosis procedure and the label "PAIN_POST" indicates the measure NRS (0-10) after the MRI procedure in hypnosis in each patient of the hypnosis group.

	"PAIN_PRE"	VS.	"PAIN_POST"
MEDIAN	0		0
RANGE	(0-10)		(0-10)

P.VALUE (WILCOXON TEST) =0.097 P<0.05 is significant

2.4 Presence of artefacts.

In order to analyze the correlation of hypnosis with the presence of artefacts, we checked all the reports of the MRI exams and measured:

1. **MRI reports with artefacts in hypnosis group:** 8 on 56 exams. The hypnosis group has a significantly higher number of artefacts compared to the anesthesia group. This has already been shown as a descriptive data. Here we show that the vein catheter insertion and the MRI field strength even if potentially disturbing did not influence the presence of artefacts.

TABLE 8: Presence of artefacts (Present=Yes; Absent=No) in the hypnosis and anesthesia group described in the reports of MRI exams

Variable		Hypnosis group		Anesthesia group	
Artefacts	No	48	(86)	50	(100)
	Yes	8	(14)	0	(-)

Fisher's exact test: p=0.005

2. **Artefacts vs. TESLA**: we found no significant correlation (**Fisher's exact test p** = 0.2408) between the MRI 3 TESLA and the presence of artefacts in the hypnosis group, leading to the conclusion that artefacts in the group hypnosis were not due to the noise and impulse of MRI 3 TESLA.

TABLE 9: ARTEFACTS vs. TESLA in hypnosis group. Presence of artefacts described in the clinical reports (Present=Yes; Absent=No) in the hypnosis group in the MRI exams performed on the 1.5 TESLA and 3 TESLA MRI machine.

TESLA	**ARTEFACT**			
	NO		**YES**	
	N	(%)	N	(%)
1.5	31	(55.36)	3	(5.36)

3	17	(30.36)	5	(8.93)

Fisher's exact test: p = 0.2408

3. **Artefacts vs. Vein:** we found no significant correlation (**Fisher's exact test**

p = 1.0000) between artefacts and the insertion of the peripheral vein catheter in the hypnosis group, leading to the conclusion that the artefacts were not due to the extra challenge of vein catheter insertion.

TABLE 10: ARTEFACTS vs. VEIN in hypnosis group. Presence of artefacts (Present=Yes; Absent=No) correlated with vein catheter insertion (Present=Yes; Absent=No) in the hypnosis group described in the reports of MRI exams.

VEIN	ARTEFACT			
	NO		YES	
	N	(%)	N	(%)

NO	29	(51.78)	5	(8,92)
YES	19	(33.93)	3	(5,38)

Fisher's exact test: p = 1.0000

Furthermore, even though performing the MRI exams in hypnosis led to more movement artefacts, no exam accomplished was not diagnostic. In 1 case of hypnosis group, an MRI exam was accomplished missing some sequences, due to the movements of the patient. The exam was still diagnostic. The anesthesia group did not show any artefact nor missing sequences. All exams were diagnostic.

2.5.Patients that stopped using anesthesia for MRI after the exam in hypnosis.

In order to analyze the difference in behavior of children after the procedure hypnosis we measured:

1. Number of patients in both groups that performed MRI exams awaken after the procedure examined (hypnosis vs. anesthesia):

We compared the data measured between hypnosis and anesthesia group and we found a significant difference in those patients that received hypnosis (Fisher's exact test: p = 0.0274), meaning that patients that received the hypnosis procedure were more likely to perform the MRI exam awaken the following time.

TABLE 11: Hypnosis group and Anesthesia group vs Subsequent exams in sedation or not. The table shows that children that received the hypnosis procedure are more likely to accomplish the next MRI exam awake.

	Not in sedation		In sedation	
	Number	(%)	Numb er	%)
Hypnosis group	52	(92,8)	4	(7.2)
Anesthesia group	38	(76)	12	(24)

Fisher's exact test

p = 0.0274

And the latter results were not related to the age of the patients as shown in the following table that compares the groups of patients of different ages that are performing the next exams awaken with those that perform the exams under anesthesia

TABLE 12: Hypnosis group post_awaken vs age < 8 years

	Age < 8y		**Age>=8y**	
	N	(%)	N	(%)
Post-awaken	26	(46.4)	26	(46.4)
Post-anesthesia	2	(3.6)	2	(3.6)

Fisher's exact test

p = 1.0000

Note. We used separation criteria (median 8 years) to emphasize the population's differences

2. Number of patients in the hypnosis group that performed MRI exams awake after the procedure and that before needed anesthesia for MRI exams.

About the number of patients in the hypnosis group that performed MRI exams awake after the procedure and that before needed anesthesia for MRI exams, we found no significant difference within the hypnosis group (**Fisher's exact test: p** = 0.6022).

TABLE 13: Comparison within the hypnosis group between patients who performed the exams after the procedure awake and those who performed them in sedation.

The label *post_awaken* indicates those patients who performed the next MRI exams awaken after the hypnosis procedure, while the label *post_sed* indicates patients who performed in sedation the next MRI exams after hypnosis. *Pre_no_sed* indicates those patients who did not make previous MRI exams in sedation, while *pre_sed* indicates those patients that made their previous MRI exams in sedation.

	Post_awaken		**Post_sed**	
	N	(%)	N	(%)
Pre_no_sed	34	(61.8)	2	(3.64)
Pre_sed	17	(30.9)	2	(3.64)

Fisher's exact test

p = 0.6022

***2.6. MRI exam duration*.** We recorded the length in minutes of all the MRI exams and compared the results between hypnosis group and anesthesia group.

We found no significant difference (**Fisher's exact test: p = 0.4339)** between the two groups (hypnosis and anesthesia) in MRI exam duration.

2.7. Unpredicted risks: We recorded those cases in which the MRI exam detected other conditions than the one investigated that might predict an increased anesthesiological risk. We found:

1 (one) mass that was compressing and dislocating the oro-pharynx

1 (one) “significant” phlogosis of the first airways

1 (one) impression of the axis on the cervical cord

V. DISCUSSION

DISCUSSION

The main aim of this study was twofold: (1) to develop a protocol based on the Ericksonian hypnotic approach to manage distress and allow steadiness during MRI exams in pediatric patients, and (2) to study the protocol's efficacy when used with pediatric patients undergoing MRI exams in a hospital setting (Tertiary Care Pediatric Hospital).

We realized a procedure that was easy to repeat, flexible, and tailored to children of different ages.

The key and the innovation of the present procedure was to prescribe movement as a symptom. The technique was never described as such and used for this scope. It can easily be repeated by personnel with efficacy.

About the protocol's efficacy, five key findings emerged:

First, hypnosis protocol was efficacious to allow steadiness in MRI and obtain reliable exams, in which movement artefacts, even if present, were not obstructive to the MRI image interpretation.

Second, hypnosis allowed to reduce procedure-related anxiety, while it was not significant in pain management.

Third, patients who received hypnosis as treatment were more likely to perform subsequent MRI exams awaken, but no significant impact was found on the change of behavioral path from anesthesia to perform the MRI exams awaken. Age did not influence those results.

Fourth, no significant difference was detected in the duration of the MRI exams performed between those who accomplished the exam in hypnosis and those who were under anesthesia.

Fifth, the amount of drug used and, as a consequence, the potential anesthesiological risk of those patients was considerably reduced.

As underlined in the introduction, studies focused on the use of hypnosis in MRI are available in adult patients, but not much is possible to find in a pediatric population (Alexander, 2012).

Our findings are consistent with previous studies showing that hypnosis is effective in reducing anxiety in MRI settings. (Benotsch et al., 2000; Lang et al., 1999), Moreover, it is useful in the pediatric population (Alexander, 2012; Liossi et al., 2006) for anxiety and procedural pain control.

Hypnosis has been effective in reducing anxiety in children (Manyande et al., 2015). It has been compared with midazolam, a short-acting benzodiazepine (Calipel et al.,2005), showing that fewer children were anxious in the hypnotherapy group than the midazolam premedication group.

Hypnosis is considered effective in controlling procedural pain with Magic Glove's technique (Kohen & Olness, 2011) even though our study results are not significant.

Here we report two studies: first, a brief report about the use of hypnosis with 2.5–4.5-year-old children with autism, developmental delays, and typical development (Nordahl et al. 2008). Investigators achieved a 93% success rate in acquiring high-quality MRI scans without the use of sedation. The primary strategy was to conduct MRIs during natural nocturnal sleep in the evenings after the child's usual bedtime. Alternatively, with some older and higher functioning children, the MRI was conducted while the child was awake and watching a video. All children were acquainted with the procedure through a complex familiarization protocol.

The second study (Bates et al., 2010) we mention is a study about a distraction technique, coping strategies, and familiarization with the MRI environment used to realize MRI scans in children between the ages 4-7 with similar results to our study. 70 patients attempted, and 5 did not succeed, more artefacts were present, but the MRI scans were still diagnostic. No study reported possible changes in the future behavior of children or used precisely the Ericksonian approach.

Our study has some limitations that should be considered when interpreting the results:

1. The low number of patients enrolled due to the system's lack of compliance.

The course about the use of hypnosis in the Radiology department carried out by the investigator had the scope to reduce the nocebo effect of personnel. The investigator wished to have an increase in the system's compliance, too, but the course was not sufficient to change the general belief that pharmacological anesthesia was more straightforward and more productive in a short time. Nevertheless, positive outputs included: that after another year from the end of the study, the hospital changed how to schedule patients, giving the children above eight years old the possibility to perform the MRI without anesthesia, and after two years, nurses and technicians expressed appreciation for hypnosis procedures.

Paradoxically most critical reasons for this “resistance” were issues non-related to hypnosis, but anesthesia, which increased personnel stress. Lang et al. (2010) put in evidence how concerns about security and workplace disruption might adversely affect the staff’s ability to project behavior that is helpful for the patient.

2. Lack of measures: the lack of time due to the organization and lack of personnel compliance made the recordings not easy.

Even though we could not improve the recording system in this circumstance, the specific challenge inspired us to implement in the future parents’ observations’ recordings. Our use of the VARS scale for anxiety, allowing parents to respond on behalf of their children, was not found in the current literature and would need further validation.

Furthermore, it will be useful to record parents’ satisfaction rates through questionnaires.

After introducing the hypnosis, the Radiology department and the Anesthesia department arranged that children above the age of eight could perform the procedure awaken. Above that age, every child had the opportunity of a meeting in the play MRI with a technician trained in communication skills in our course.

The previous policy of the hospital was to schedule in anesthesia all children below ten years old.

The positive impact of this change is complex.

To understand its extent, we must address the risks, the complications, and the side effects of using drugs in general sedation in a hazardous environment outside the operating rooms (NORA: Non-Operating Room Anesthesia).

We can start by mentioning the most common side effect of the drug that was at most limited in its use: sevoflurane.

Inhalation of halogenates (especially sevoflurane and desflurane) is considered responsible for an altered state of consciousness that manifests as a psychomotor reaction with disorientation and hyperactivity at the awakening of anesthesia, in particular in children. This condition is known as Emergence delirium (ED). It is more common in preschool-aged children, and its incidence varies between 10 and 80% in children. These events are often short-lived, but they increase the risk of self-injury and delayed discharge, require additional nursing staff, and increase medical care costs, all of which are causes for concern. Physiological factors, pharmacological factors, the type of procedure, the anesthetic agent administered, painful stimuli, and various patient factors can all contribute to ED (Moore &Anghelescu, 2017).

The hypnosis group did not experience delirium.

Instead, only one patient had psychomotor agitation and recovered a few minutes after speaking to the child. He was a deaf child of 8 who was prepared with hypnosis; at the beginning of the exam, he wanted to leave the MRI room and was agitated. After speaking with him, it was clear that the problem was the poor tailoring of the technique. The MRI’s noise that the patient could hear during the explanation with the hearing aid had become, after taking it off (because not compatible with the magnetic field), only a kinesthetic sensation that the researcher did not appropriately tailor.

In terms of morbidity and mortality, few more words are mandatory.

Very little published data are available on NORA-related mortality and morbidity.

Melloni listed all potential problems that can arise with NORA: death, hypothermia, aspiration of gastric content, hypovolemia, airway difficulties, anaphylaxis, postoperative nausea and vomiting, procedure-related complications, harm to the anesthetist (waste inhalational anesthetics, radiation exposure, exposure to the electromagnetic field) to mention some.

Robbertze et al. (2006) noted that mortality was increased with NORA as opposed to conventional operating room anesthesia. These authors' further observation was that many complications could have been prevented with better monitoring (Van De Velve et al., 2009).

Cravero et al. (2006) reported the incidence and nature of adverse events occurring in NORA in over 30 000 pediatric patients. No deaths occurred. Cardiopulmonary resuscitation was required once. The most prominent type of complication was respiratory-related. Once per 89 NORA procedures resulted in events that could have been potentially harmful if timely rescue was not performed. Respiratory events were frequent, and adequate monitoring essential. Especially in very young patients, respiratory events are a large proportion of all events reported.

According to Kakavouli et al. (2009), the average risk for performing general anesthesia in children is the same as non-operating room anesthesia and not more or less. Intraoperatively higher incidence of AE is observed in children with higher ASA status (ASA status= American Society of Anesthesiologists' classification system that estimates the preoperative risks related to the patient's health condition before surgery) or younger age irrespective of location or under scheduled nature of the procedure. The majority of AE were because of respiratory causes, irrespective of location.

Little has been published about mobility and mortality in hypnosis: psychotic derailment in patients with borderline personalities and rhythm disturbances due to increased parasympathetic system tone (Scagnelli, 1976; De Benedittis et al., 2018).

After comparing the mobility and mortality data in both procedures, hypnosis shows a better safety profile. It allows us to avoid those conditions that are not detected before the MRI procedure, which can lead to unpredictable complications.

All those considerations are difficult to translate in numbers with our little observational study. Much more data are necessary.

VI. CONCLUSIONS

CONCLUSIONS

We developed a novel hypnotic procedure created to help children and adolescents undergo MRI without anesthesia. Its originality lies in prescribing the movement as a symptom and its efficacy in tailoring both patient and MRI procedures. In particular, this hypnotic protocol can be used even when the hypnotist is busy during the MRI procedure because it uses the noise and the environment of MRI to deepen and eventually reinduce trance when the trance state of the patient is more superficial. It is easily adapted to a different type of MRI exams, using the district of investigation as a guide to tailor the procedure, prescribing the "symptom movement" far from the area that has to be investigated with the MRI. Its flexibility and structure consent to having both tailoring and a standard procedure, and it can be adopted for clinical practice and further experimental studies.

This preliminary study has shown that the newly created hypnotic procedure can be used to control anxiety and allow children to accomplish MRI exams without anesthesia, which in turn increases the exam's safety considerably. Also, patients in the hypnotic procedure accomplished the next MRI exams without sedation significantly more often than the anesthesia group. Children's capability to apprehend new skills and extend their applicability to new contexts can explain the change in the observed behavioral pattern in the next MRI exams after the procedure in hypnosis. This fact increases the beneficial effects of the hypnosis protocol. If these results are confirmed in future research, it will favor recommending the procedure as standard care.

VII. REFERENCES

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VIII. SUPPLEMENTARY MATERIALS

SUPPLEMENTARY MATERIALS

1. A functional definition of pharmacological anesthesia and hypnosis: from phenomena to an underlying substrate

Facco (2016) stated that the neurophysiological effects of hypnosis are the basis of its relevant effect in the anesthesiology field (Facco, 2016).

We present some details about the neurophysiology underlying pharmacological anesthesia and hypnosis in order to have a deeper insight into the efficacy of the two techniques and a deeper understanding of the brain areas involved.

Studies with Functional Magnetic Resonance Imaging (fMRI) have allowed us to investigate the functional and anatomical substrate in the brain of the clinical manifestations obtained through anesthesia and hypnosis.

About how anesthetic agents can suppress consciousness, substantially, these drugs (i.e., propofol, halothane, isoflurane, sevoflurane, xenon, clonidine, lorazepam, midazolam) reduce cerebral metabolic activity and blood flow with some degree of heterogeneity depending on the agent. These drugs collectively reduce neuronal activity in different regions with a corresponding effect on regional cerebral blood flow (rCBF). To be precise, however, some regions have an increase, and others an activity decrease: the Thalamus is among the areas that decrease activity, and the Anterior Cingulate Cortex (ACC) and the Insula have an increase (Ramani & Wardhan, 2008). At present, there is mounting literature supporting the hypothesis that the deactivation of the Thalamus and the loss of cortical thalamus connectivity are at the base of hypnosis induced by anesthesia (Alkire et al., 2000; Alkire et al., 2005; Bonhomme et al., 2001; Bonhomme et al., 2008; Fiset et al., 1999; Kaisti et al.,2003; Ramani et al., 2007; Schlünzen et al., 2006; Schlünzen et al., 2004; Veselis et al., 2003).

Electrophysiologically, this seems to be accompanied by the transition from alpha waves of 7-14 Hz originated in the Thalamus to delta waves (1-4Hz) (Franks et al., 2008; Schreckenberger et al., 2004).

It has been shown that in addition to the reduction of activity, a global effect of disconnection of neuronal activity is needed to be able to perceive functional alterations such as amnesia and narcosis (Ramani & Wardhan, 2008).

Loss of connectivity has been demonstrated in some neurological diseases affecting white matter, such as Alzheimer's disease and Multiple Sclerosis. (Rombouts et al., 2005)

At present, no consensus has emerged regarding the neurological mechanism by which anesthetic agents modulate consciousness. The changes observed in functional connectivity during the induction of anesthesia do not reflect the same observed in the emergency from anesthesia; the awakening from anesthesia could involve an increase in functional connectivity higher than the awakening baseline. (Hudetz, 2012)

Anesthesia allows consciousness suppression but also pain control. Regarding *pain*, given its multidimensional nature (sensory, affective, cognitive, and motor component discrimination), different regions appear to be activated by the pain stimulus and are therefore modulated by anesthetics and hypnosis. These regions can be divided into the Medial Pain System and the Lateral Pain System.

The Medial System includes the Anterior Cingulate Cortex (ACC), the Amygdala, the Hippocampus, the Hypothalamus, the Spino-reticular projections, the Locus Coeruleus, and the Spino-mesencephalic projections to the Periaqueductal gray. (Bourne et al., 2014; Kupers & Kehlet, 2006). It is associated with the emotional, motivational, and cognitive components of pain, while the Lateral Pain System (primary and secondary somatosensory cortex, Insula, and parietal Operculum) controls the discriminatory sensory aspect of pain.

Some studies carried out using Positron Emission Tomography (PET) suggest that opioids generate analgesia by acting primarily on the medial system of pain. It appears that opioid-mediated analgesia decreases neuronal activity in regions associated with pain perception and increases nerve activity in regions/circuits related to pain modulation (Wagner et al., 2007).

Furthermore, in addition to the observed functional changes, structural changes have been observed in individuals with chronic pain: a loss of gray matter and a reduction in cortical thickness in specific regions. (Iadarola et al., 1995). These regions are the same identified in the processing of the pain stimulus. This loss can be determined both by chronic glutamatergic excitotoxic activity and by lifestyle changes due to pain. The loss of gray matter in the Parahippocampal gyrus and the Frontal cortex could be related to cognitive deficits connected with chronic pain (Ramani & Wardhan, 2008; Siddall et al., 2006).

The other two endpoints of anesthesia are *amnesia* and *suppression of motor reflexes*. The attention of the studies has turned more into amnesia. It appears that numerous studies in humans and animals point to the Temporal Medial cortex that includes the Hippocampus as a primary site in the control of episodic memory. However, functional studies refute this position indicating only the activation of memory in the activation of the Prefrontal cortex and not of the Hippocampus (Veselis, 2003)

Hypnosis, according to fMRI (Functional Magnetic Resonance Imaging) and PET (Positron Emission Tomography):

Concerning neuroimaging studies that seek to clarify the mechanisms underlying hypnosis, it is necessary to point out a significant inconsistency in the findings.

The multifaceted nature of hypnosis and the lack of a consistent research methodology have generated an inevitable heterogeneity of results.

An essential ability of the human brain is to be able to switch between different tasks rapidly, and it seems that behind this skill, there are interactions between different networks of the brain, the same networks that are involved in the mechanisms of hypnosis. Briefly, we can define the structure of the networks involved in the mechanisms of hypnosis and how they connect.

TheCentral Executive Network (CEN), the Salience Network (SN), and the Default Network (DN) appear to be the critical networks implicated in hypnotic susceptibility, hypnotic induction, and response to hypnotic suggestions (Landry et al., 2017).

The CEN is involved in higher-order cognitive and attention control. It is related to the Posterior Dorsolateral Prefrontal and Parietal cortex and has a subcortical coupling different from the SN (Menon, 2011). The SN is an intrinsically connected large-scale network that is distinct from the dorsal attention network anchored in the frontal eye field and intraparietal sulcus and the left and right lateral frontoparietal central executive networks. It has distinct patterns of intrinsic cortical and subcortical connectivity from the lateral frontoparietal central executive network in the anterior thalamus (antTHAL), dorsal caudate nucleus (dCN), dorsomedial thalamus (dmTHAL), hypothalamus (HT), periaqueductal gray (PAG), putamen (Put), sublenticular extended amygdala (SLEA), substantia nigra/ventral tegmental area (SN/VTA), and temporal pole (TP). Those specific connections are significant for the salience of external stimuli and internal brain events. The SN is anchored in the AI (Anterior Insula) and ACC (Anterior Cingulate Cortex) and presents extensive connections with the subcortical and limbic structures involved in reward and motivation (Menon, 2015).

The DN (Default Network) includes the Temporal Medial lobes and the Angular Gyrus (AG), the Posterior Cingulate Cortex (PCC), and the Frontal Ventromedial Cortex (VMPFC). These areas perform a wide variety of functions: the PCC is involved in autobiographical memory, the VMPFC is associated with social cognitive processes that affect ourselves and others; the Temporal Medial lobes are involved in episodic and autobiographical memory (Menon, 2011).

The SN plays a crucial role in dynamic switching between the central executive and default-mode networks. The SN recruits the central executive and task control regions to maintain cognitive set and manipulate information in working memory while suppressing the default-mode network to keep attention focused on task-relevant goals (Menon, 2015).

The activity and connectivity both within and between these higher-order networks seem to support mental absorption and facilitate the implementation of top-down strategies to produce hypnotic responses. Besides, they can help reduce attention to extraneous events and decrease episodes of mind wandering. However, a recent review and meta-analysis (Landry at al., 2017), rather than confirming the role of these higher-order networks, revealed that hypnotic responses correlate robustly with the activation of the Lingual gyrus, probably related to mental imagery. Studies are still needed to explore, for example, hypotheses different from the top-down model of hypnosis (Landry at al., 2017).

Facco (2016) specifies that relaxation and absorption of hypnosis lead to activation of the Anterior Cingulate Cortex (ACC), Motor Cortex, and Somatosensory Cortex and determine a reduction in perfusion of the temporal lobes. Relaxation is also accompanied by an increase in perfusion of the Occipital cortex and a reduction in perfusion in the Brainstem, Cerebellum, Thalamus, Basal nuclei, and Prefrontal cortex, while absorption is accompanied by an increase in perfusion at the level of the Brainstem, the Prefrontal cortex and a reduction in occipital perfusion. Thus hypnotic relaxation and absorption are entirely distinct.

Hypnosis is a complex dynamic activity where a wide range of brain patterns can be found depending on specific activities. Facco emphasizes the role of the Anterior Cingulate Cortex (ACC) as an area activated by hypnosis and a crucial area in the perception of pain, in the monitoring of the conflict between incongruent stimuli, excitement (arousal), attention, cognition, emotion, motivation and movement control.

The mitigating effect of hypnosis on *the pain threshold* and the subjective experience of the pain stimulus have been validated and studied in volunteers as reviewed by Wobst, 2007. In these studies, the pain was elicited by stimulating the supraorbital nerve, dipping the hand in cold water, or using a tourniquet around the arm, and was significantly reduced with hypnosis, and it was not possible, when administered, to reverse the effect of hypnosis with naloxone (opioid antagonist). Hyperalgesia was also evoked by specific suggestions, and although there was a positive response to the suggestions, the somatosensory and auditory evoked potentials, and the electroencephalogram remained unchanged. The investigators also did not observe changes in plasma concentrations of endorphins and adrenocorticotropic hormone. Continuous suggestions during the pain stimulus improved the effect of the suggestions given before the application of the painful stimulus (Wobst, 2007).

Imaging studies using Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) and studies on evoked potentials in response to pain stimuli have improved our knowledge of nerve circuits involved in pain. Specific alterations in the metabolic activity and perfusion of the anterior cingulate gyrus have been demonstrated to be related to pain. Significant changes in the perception of pain during hypnosis seem to be due to inhibitory feedback from the anterior frontal cortex or the anterior cingulate cortex on cortical thalamus activity. In particular, since the rostrum and the genu of the corpus callosum serve as a bridge between the frontal cortices, they can be crucial in exerting attentional and inhibitory control and influencing the efficacy of the frontal cortex in acting as a sensory gate (Wobst, 2007). Medial and lateral prefrontal and parietal cortices are considered hubs of network regulation (Raichle, 2011), and this can be of interest in pain management (Jensen et al., 2017).

Recent studies show a possible role of cerebellum in hypnosis suscettibility (Santarcangelo & Scattina, 2016) and pain modulation (Bocci et al., 2016).

The underlying physiological mechanisms guide the hypnotist in choosing the appropriate approach.

A new frontier and challenge is the introduction of quantum physics as a paradigm of explanation of the mind functioning and the efficacy of hypnosis as a treatment. Conscious states may be conceptualized as a continuum spectrum from high order consciousness to an altered state of consciousness. Hypnosis and its techniques may be reframed through quantum mechanics phenomena. (De Benedittis, 2020). Studies that would start from that theoretical assumption might finally cross the fictional boundaries between body and mind.