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# Review article

# Hypnosis as a non-pharmacological intervention for invasive medical procedures - A systematic review and meta-analytic update

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#### ABSTRACT

Hypnosis is recognized as an effective non-pharmacological intervention for managing anxiety, pain, and physiological stress during invasive medical procedures. Despite its growing use, variability in techniques and inconsistent outcome measurements have challenged its clinical standardization. This systematic review and meta-analysis evaluated the effectiveness of hypnosis in reducing anxiety, pain, and physiological stress during invasive procedures, while identifying the most effective techniques as well as assessing analgesic use and safety. A comprehensive literature search was conducted in PubMed, Cochrane Library, and Scopus to identify randomized controlled trials (RCTs) evaluating hypnosis in invasive procedures. Eligible studies were assessed for bias using the Revised Cochrane Risk of Bias Tool. Meta-analyses were performed with a random-effects model, and subgroup analyses were conducted based on hypnosis techniques, patient characteristics, and procedure types. Twenty RCTs with 1250 patients were included. Hypnosis significantly reduced anxiety (SMD =-0.43, 95% CI: -0.58 to -0.28, p < 0.001) and pain (SMD = -0.35, 95 % CI: -0.50 to -0.20, p < 0.001) compared to standard care. Subgroup analyses indicated that virtual reality-enhanced hypnosis and tailored interventions for high-anxiety procedures were most beneficial. Physiological stress markers, including heart rate and blood pressure, were also reduced, supporting the calming effects of hypnosis. Adverse effects were minimal. Hypnosis is effective and safe for reducing anxiety and pain during invasive medical procedures. Standardized protocols and further research are needed to optimize its clinical use and enhance adoption in routine care.

# 1. Introduction

Hypnosis has been increasingly recognized as a valuable non-pharmacological intervention to manage pain and anxiety during invasive medical procedures [1]. This approach, often referred to as hypnotic analgesia, involves guiding patients into a state of focused concentration and heightened suggestibility, allowing them to respond to suggestions that can alter their perception of pain and anxiety [2,3]. The therapeutic use of hypnosis in medical settings dates back decades, but recent advancements in neuroimaging and clinical research have further elucidated its mechanisms and efficacy [4,5].

A growing body of literature supports the efficacy of hypnosis in various clinical contexts. A meta-analysis by Tefikow et al. (2013) involving 34 randomized controlled trials (RCTs) with 2597 patients

undergoing medical interventions found that hypnosis significantly reduced pain (Hedges' g=0.44) and emotional distress (Hedges' g=0.53) compared to standard care [6]. This was updated by Holler and colleagues in 2021 incorporating 50 RTCs with 4269 adult patients undergoing surgical procedures. Their findings confirmed significant reductions in pain (g=0.37), mental distress (g=0.55), and medication consumption (g=0.46), though effects on physiological parameters were not significant. [7].

Additional reviews consistently show hypnosis outperforms standard care and attention controls, and is comparable to other psychological interventions [8,9]. Noergaard et al. (2019) emphasized the impact of hypnosis in minimally invasive procedures, reporting a significant reduction in analgesic consumption without exacerbating pain or anxiety, which has notable implications for patient safety and recovery [10].

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While not confirmed in other studies [7], hypnosis has also been shown to modulate physiological responses, such as heart rate and blood pressure, both of which are critical indicators of autonomic nervous system activity during medical procedures. Fernandez et al. (2021) conducted a scoping review examining the effects of hypnosis on psychophysiological parameters, concluding that hypnosis is associated with lower sympathetic activation, reduced cardiovascular stress responses, and overall autonomic regulation [11]. Another critical aspect of hypnosis research is its safety profile and potential adverse effects. Although hypnosis is generally regarded as a low-risk intervention, a recent international survey of 691 clinicians from 31 countries found that 55 % of practitioners had encountered hypnosis-associated adverse effects, though these were typically mild and transient (e.g., dizziness, nausea, or transient confusion) [12].

Despite these promising findings, significant variability exists in the techniques and implementation of hypnosis across studies, which poses challenges for its standardization and broader adoption in clinical practice. Differences in delivery methods—ranging from traditional verbal suggestions to innovative approaches such as virtual reality-enhanced hypnosis—lead to inconsistencies in outcomes, complicating the ability to draw generalized conclusions about the most effective approaches. The impact of hypnosis also appears to vary by patient characteristics and the type of procedure [12].

However, current meta-analyses often lack detailed subgroup analyses and do not adequately address the methodological variability across studies, leading to gaps in understanding the optimal implementation of hypnosis. Additionally, the evolving landscape of hypnosis techniques, including the introduction of digital and virtual reality-based interventions, has not been fully explored in the context of recent clinical research [13,14]. There is a critical need for an updated and comprehensive meta-analysis that systematically evaluates these variables, providing clear evidence to guide the integration of hypnosis into routine clinical practice.

Therefore, the primary aim of this systematic review is to assess the impact of hypnosis on pain and anxiety during invasive medical procedures. Secondary aims include evaluating its effects on physiological parameters such as heart rate and blood pressure and exploring any reported adverse reactions related to hypnosis. Further, this analysis will systematically evaluate various hypnosis methods, including traditional verbal suggestions, guided imagery, and virtual reality-enhanced hypnosis, to determine which techniques are most effective in specific procedural contexts.

#### 2. Methods

# 2.1. Search strategy, study selection and data extraction

A systematic literature search was conducted in databases including PubMed, Web of Science, Cochrane Library, and Scopus to identify RCTs published between 01.01.2006 and 30.12.2025 that evaluated the effectiveness of hypnosis during invasive medical procedures. The search included the keywords "hypnosis" OR" hypnotic analgesia" AND "invasive procedures" OR "surgical procedure" OR "medical procedure" AND "pain" OR "pain management" OR "analgesia" AND "anxiety" OR "stress" (Supplementary material). Studies were included if they investigated the effects of hypnosis as an intervention on the same day of the invasive procedure. Eligible studies enrolled adult participants (≥18 years old) undergoing invasive medical procedures such as surgical interventions, interventional radiology, or endoscopic procedures. Only randomized controlled trials with a control group were considered, and studies had to report quantitative outcome measures related to pain, pain management, analgesia, anxiety, or stress. Furthermore, only studies published in English in peer-reviewed journals within the specified time frame were included. Exclusion criteria included studies focusing on pediatric populations, and secondary data analyses from previous published trials (e.g., [15]). Two reviewers (NW, MLT)

independently screened titles, abstracts, and full texts, resolving disagreements through discussion. One full text could not be retrieved [16]. This review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [17].

Data were extracted on study characteristics, patient demographics, type of procedure, hypnosis intervention, control group conditions, outcome measures (anxiety, pain, physiological parameters), and adverse reactions. Specific data points included means, standard deviations, and sample sizes for both intervention and control groups (please see Table 1 for details).

#### 2.2. Meta-analysis

Pooled analyses were performed using a random-effects model due to expected variability between studies. The primary outcomes were anxiety and pain scores, measured using standardized tools like the Spielberger Anxiety State Inventory [18] and Visual Analog Scale (VAS) for pain [19]. The effect sizes were calculated as standardized mean differences (SMD) to allow comparisons across different measurement scales. A random-effects model was chosen to pool the SMDs, accounting for heterogeneity among studies due to variations in hypnosis techniques, patient populations, and procedural contexts. This model assumes that the true effect size varies between studies and provides more conservative estimates than fixed-effects models. Heterogeneity was assessed using the I<sup>2</sup> statistic, which quantifies the proportion of variance due to study differences rather than random error. A high I<sup>2</sup> suggests substantial heterogeneity, supporting the use of random-effects modeling. The pooled SMDs were computed using SPSS Statistics v. 28.0 (IBM, USA) along with 95 % confidence intervals to reflect the precision of the estimates. Statistical significance was assessed using p-values to determine the overall impact of hypnosis on anxiety and pain reduction. The level of significance was set at p < 0.05.

To explore potential sources of heterogeneity and assess the differential effectiveness of hypnosis, subgroup analyses were conducted based on predefined criteria. The subgroups were determined a priori, based on established literature and clinical relevance, and were stratified according to the following key factors: type of hypnosis technique (traditional verbal suggestions, guided imagery, and eye fixation vs. virtual reality-enhanced hypnosis vs. audio-recorded hypnosis), type of medical procedure (cardiac and vascular interventions vs. minor surgical procedures vs. diagnostic procedures), and baseline anxiety levels (high vs. low to moderate). Each subgroup analysis was conducted to assess whether the effect sizes varied significantly across these categories and to provide insights into the optimal conditions and patient populations for hypnosis interventions.

#### 2.3. Risk of bias assessment

The risk of bias was evaluated using the Revised Cochrane Risk of Bias (RoB 2) Tool, assessing randomization, allocation concealment, blinding, incomplete outcome data, and selective reporting [20]. Studies were classified as low, high, or unclear risk of bias.

#### 3. Results

#### 3.1. Study characteristics

The meta-analysis included 20 RCTs involving a total of 1250 patients (Fig. 1, Table 1). The studies covered a diverse range of invasive medical procedures, including peripheral endovascular interventions, cardiac surgeries, lumbar punctures, coronary angiography, cystoscopy, and various other surgical and diagnostic procedures. Hypnosis interventions varied across studies, utilizing techniques such as verbal suggestions, visual imagery, guided imagination, Ericksonian hypnosis, and virtual reality-enhanced hypnosis. Control groups included standard

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Table 1 Extracted data.

|     | Author, year                                 | Indication                                 | Number of patients, ratio male/female in percent, average age in years   | Control group: number<br>of patients, ratio male/<br>female in percent,<br>average age in years,<br>procedure | Hypnosis intervention  | Duration and<br>time point of<br>hypnosis<br>intervention  | Outcome measure  | Time of outcome assessment                 | Result   | Adverse<br>reactions<br>related to<br>hypnosis<br>intervention |
|-----|--|--|--|---|--|--|--|--|--|--|
| 1   | Gullo et al.,<br>2023<br>[24]                | Peripheral<br>endovascular<br>intervention | n = 50,<br>42/58,<br>48.9 ± 17.1   | n = 50,<br>58/42,<br>$45.8 \pm 16.6,$<br>SOC  | Virtually augmented self-hypnoses                                    | Individual,<br>during procedure                            | Spielberger Anxiety<br>State Inventory<br>VAS pain   | Directly after                             | Difference pre-post $6.96 \pm 10.03$ vs. $11.16 \pm 9.23$ , $p < 0.001$ $2.04 \pm 1.82$ vs. $2.62 \pm 2.42$ , $p$                                | dizziness, face<br>sweating in 2<br>patients (4 %)             |
| 2   | Rougereau<br>et al., 2023<br>[33]            | Percutaneous hallux valgus surgery         | n = 30, 3/97, 55 ± 13  | n = 30,<br>10/90,<br>$52 \pm 15,$   | virtual reality<br>hypnosis mask                                     | 10 min, directly before                                    | State Trait Anxiety<br>Inventory<br>Use of ketamine  | postoperative                              | = $0.33$<br>42.5 $\pm$ 9.7 vs. $45.2 \pm$ 7.9, $p$ = $0.04$  | None reported  |
| 3   | Abensur<br>Vuillaume<br>et al., 2022<br>[23] | Coronary<br>angiography                    | n = 85,<br>68/32,<br>66 (range<br>44–91)   | SOC<br>n = 84,<br>64/36,<br>68 (range 38–88),<br>placebo,<br>conversational                                   | visual induction and catalepsy techniques                            | 15 min, directly before                                    | Spielberger Anxiety<br>State Inventory<br>VAS pain   | Preoperative                               | 3.3 % vs 26.6 %, <i>P</i> < 0.03<br>45 vs. 46, <i>p</i> = 0.23   | None reported  |
| 4   | Rousseaux<br>et al., 2022<br>[34]            | cardiac surgery                            | n = 18<br>hypnosis,<br>72/28,<br>$67.6 \pm 12.5$<br>n = 15 VR<br>76/24,<br>$64.7 \pm 13.4$<br>n = 15 VR+<br>hypnosis<br>84/16, | interview $n = 22$ , $72/28$ , $63.3 \pm 11.5$ , SOC  | verbal suggestions<br>guided imagination                             | 20 min, day<br>before and after<br>surgery,<br>prerecorded | Anxiety, pain,<br>fatigue, relaxation,<br>opioid use, heart<br>rate, arterial<br>pressure,<br>respiratory rate,<br>pupil size and<br>oxygen saturation | postoperative<br>Pre- and<br>postoperative | VAS $\geq$ 4: 1 vs. 3, $p=0.37$<br>No significant differences<br>between the groups  | None reported  |
| 5   | Courtois-<br>Amiot et al.,<br>2022<br>[35]   | Lumbar puncture                            | $68.4 \pm 7.8$<br>n = 25,<br>40/60,<br>$77.0 \pm 5.2$ ,<br>cognitively<br>impaired   | $n=25,$ 52/48, 77.4 $\pm$ 4.8, cognitively impaired, SOC  | Hypnotic suggestions, in person                                      | 8 min, during<br>procedure                                 | VAS anxiety self and<br>hetero assessed<br>VAS pain hetero   | During<br>intervention                     | $2.3 \pm 4.9 \; \mathrm{bpm} \; \mathrm{vs.} \; 6.3 \pm 5.9, p$ $< 0.05$ 1 vs. $3, p < 0.05$   | None reported  |
|     |  |  |  |   |  |  | assessed   |  | 2 vs. 3, $p = 0.15$<br>1 vs. 2, $p < 0.05$   |  |
| 202 | Tezcan et al.,<br>2021<br>[36]               | Rigid cystoscopy                           | ppy $n = 45$ , $n = 45$ , $100/0$ , $100/0$ , $64.5 \pm 7.5$ $63.9 \pm 6.8$ , SOC  | $100/0$ , $63.9 \pm 6.8$ ,  | eye fixation, breathing<br>technique, visual<br>imagery, suggestions | 15 min, 10 min<br>before procedure                         | State-Trait Anxiety<br>Inventory<br>VAS pain<br>self and hetero<br>assessed  | End of procedure                           | $37.8 \pm 2.3$ vs. $39.6 \pm 3.4$ , $p = 0.006$<br>$7.7 \pm 1.5$ vs $8.4 \pm 1.2$ , $p = 0.027$<br>$8.6 \pm 0.8$ vs. $7.4 \pm 1.1$ , $p < 0.027$ | None reported  |
|     |  |  |  |   |  |  | MAP<br>Heart rate  | After insertion of cystoscope              | 0.001<br>$88.4 \pm 5.9 \text{ vs. } 94.9 \pm 7.9 $ mmHg, $p < 0.001$   |  |

Table 1 (continued)

|    | Author, year                                 | Indication                      | Number of patients, ratio male/female in percent, average age in years | Control group: number of patients, ratio male/female in percent, average age in years, procedure | Hypnosis intervention  | Duration and<br>time point of<br>hypnosis<br>intervention | Outcome measure  | Time of outcome<br>assessment                | Result   | Adverse<br>reactions<br>related to<br>hypnosis<br>intervention |
|----|--|---------------------------------|--|--|--|---|--|--|--|--|
| 7  | Garcia et al.,<br>2020<br>[22]               | Atrial flutter ablation         | $n = 56,$ $77/27,$ $69.6 \pm 11.7$                                     | n = 57,<br>81/19,<br>69.4 ± 12.2   | Ericksonian hypnosis<br>via headphones                       | During procedure  | VAS anxiety  | 45 min after                                 | $77.0 \pm 8.8$ vs. $91.6 \pm 5.9$ bpm, $p < 0.001$ $1.5 \pm 2.2$ vs. $2.5 \pm 3.2$ , $p = 0.16$  | None reported  |
|    | [22]   |                                 |  | placebo  |  |   | VAS pain   |  | 4.0 $\pm$ 2.2 vs. 5.5 $\pm$ 1.8, $p < 0.001$   |  |
|    |  |                                 |  |  |  |   | Use of morphine  |  | $1.3\pm1.3$ mg vs. $3.6\pm1.8$ mg, $p<0.001$   |  |
| 3  | Fusco et al.,<br>2020                        | Peripheral intravenous          | <i>n</i> = 89, 46/54,  | n = 91, neutral, 40/60,  | Ericksonian hypnosis   | <5 min, during procedure                                  | VAS pain   | Directly after                               | 1.5 $\pm$ 1.9 vs. 3.5 $\pm$ 2.3 and 3.8 $\pm$ 2.5, $p < 0.001$   | None reported  |
|    | [37]   | cannulation                     | 56.2 (range:<br>22–89)   | 53.7 (range: 18–86)<br>n = 92, nocebo,<br>48/52,<br>53.7 (range: 19–87)                          |  |   | VAS anxiety<br>VAS comfort   | Pre- and<br>postoperative                    | Pre post difference $-2.1$ vs. 0 and $+$ 0.1, ns $+1$ vs0.9 and $-$ 1.1, ns  |  |
| P  | Sánchez-<br>Jáuregui<br>et al., 2019<br>[38] | Breast biopsy                   | n = 58,<br>0/100,<br>$48 \pm 10$                                       | $n = 55,$ $0/100,$ $45 \pm 11,$ Music $n = 57,$  | Audio recorded with background music                         | 17 min, directly<br>before                                | VAS anxiety,<br>depression, stress,<br>pain and optimism                           | Pre- and post<br>intervention                | reduction in the stress ( $p < 0.001$ , $\eta 2 p = 0.06$ ); pain, ( $p < 0.01$ , $\eta 2 p = 0.04$ ); anxiety, ( $p < 0.001$ , $\eta 2 p = 0.07$ ) and denession, ( $p < 0.001$ , $\eta 2 p = 0.05$ ) in hypnosis and music | None reported  |
|    |  |                                 |  | n = 37,<br>0/100,<br>$48 \pm 12$ ,<br>SOC  |  |   |  |  | groups compared with the control group.  |  |
| 10 | Lee et al.,<br>2019<br>[39]                  | Total knee<br>arthroplasty      | n = 8,<br>13/87,<br>65.6 $\pm$ 9.3                                     | $n=8,$ psychoeducation, 13/87, 56.3 $\pm$ 11.2 $n=8,$ 0/100, 67.9 $\pm$ 10.4, SOC                | Audio recorded   | 35 min, pre- and<br>postsurgery                           | VAS pain   | 1 h after                                    | $1.25 \pm 0.8 \text{ vs } 1.95 \pm 0.7 \text{ and}$ $2.38 \pm 1.9, p = 0.907$  | None reported  |
| 11 | Hoslin et al.,<br>2019<br>[40]               | Venous access port implantation | $n = 77$ cancer patients, 47/63, 61.0 $\pm$ 13.0                       | $n=71$ cancer patients, 48/62, 57.3 $\pm$ 14.1, SOC  | Audio recorded   | 26 min, during  | Evan-LR<br>Heart rate<br>difference pre-post<br>VAS anxiety<br>difference pre post | 4 h after                                    | $78 \pm 14$ vs. $71 \pm 17$ ), $p = 0.006$<br>2 vs. $5$ , $p = 0.46$<br>2.3 vs. $2$ , $p = 0.35$   | None reported  |
| 12 | Efsun<br>Ozgunay<br>et al., 2019             | Open<br>septorhinoplasty        | $n=11, \ 55/45, \ 25.6 \pm 5.2$  | $n=11, \ 55/45, \ 25.6\pm 10.2,$   | Eye fixation,<br>deepening and<br>relaxation suggestions     | Three session: 3<br>days, one day<br>prior surgery        | Tramadol use<br>Heart rate, MAP<br>VAS pain  | After surgery                                | 1 vs 5, $p = 0.149$<br>No difference   | None reported  |
|    | [41]   |                                 |  | SOC  |  | (each 40 min),<br>day of surgery<br>(20 min)              | •  | Intraoperative<br>2 and 3 h after<br>surgery | Lower in experimental group $(p = 0.028, p = 0.047)$   |  |
| 13 | Joudi et al.,<br>2016<br>[42]                | Laparoscopic cholecystectomy    | $n = 60,$ $13/86,$ $43.1 \pm 14.4$                                     | $n = 60,$ $13/86,$ $43.2 \pm 9.4,$   | verbal suggestions<br>guided imagination,<br>audio recording | 15 min, during procedure                                  | VAS abdominal pain Use of analgesics   | 2 h after surgery                            | Lower in experimental group, $p = 0.005$   | None reported  |
|    | [ 14]  |                                 | 10.1 ± 17.7  | 43.2 ± 9.4,<br>SOC   | addio recording  |   | ose of analycores  |  | No difference, $p = 0.8$   |  |
|    |  |                                 |  |  |  |   | LOS  |  |  |  |

|    | Author, year                   | Indication  | Number of<br>patients, ratio<br>male/female in<br>percent,<br>average age in<br>years | Control group: number<br>of patients, ratio male/<br>female in percent,<br>average age in years,<br>procedure | Hypnosis intervention   | Duration and<br>time point of<br>hypnosis<br>intervention | Outcome measure   | Time of outcome assessment       | Result   | Adverse<br>reactions<br>related to<br>hypnosis<br>intervention |
|----|--------------------------------|---|---|---|---|---|---|----------------------------------|--|--|
| 14 | Akgul et al.,<br>2016<br>[43]  | Coronary artery<br>bypass grafting                  | $n = 22,$ $77/23,$ $54.2 \pm 10.2$  | n=22,82/18<br>55.0 $\pm$ 8.8,<br>placebo conversation   | Ericksonian hypnosis  | 30 min, before  | State-Trait Anxiety<br>Inventory<br>Becks Depression<br>Inventory<br>VAS<br>Use of analgesics | After hypnosis 4 h after surgery | $29.20 \pm 1.9 \text{ h vs. } 36.40 \pm \\ 14.97 \text{ h}, p = 0.003 \\ 31.9 \pm 4.9 \text{ vs. } 48.9 \pm 10.2, p < \\ 0.001 \\ 4.6 \pm 3.5 \text{ vs. } 14.1 \pm 6.5, p < \\ 0.001 \\ 0.91 \pm 1.3 \text{ vs. } 1.14 \pm 1.2, p = \\ 0.01$  | None reported  |
| 15 | Corman<br>et al., 2016<br>[44] | Trans-oesophageal<br>echocardiography               | $n = 47,$ $66/34,$ $60 \pm 15$  | $n = 51,$ $57/43,$ $55 \pm 14,$ SOC   | general relaxation,<br>specific suggestions   | 30 min, same day  | VAS discomfort  | Directly after                   | remifentanil (34.4 $\pm$ 11.4 vs. 50.0 $\pm$ 13.6 mg) and morphine (4.9 $\pm$ 3.3 vs. 13.6 $\pm$ 2.7 mg, $p$ = 0.001) 6 vs. 7 $p$ = 0.046  | None reported  |
| 16 | Hizli et al.,<br>2015<br>[45]  | transrectal<br>ultrasound-guided<br>needle biopsies | n = 32,<br>100/0,<br>$63.5 \pm 6.1$   | $n = 32$ , $100/0$ , $61.8 \pm 6.8$ , placebo conversation  | relaxation-based<br>induction, guided<br>imagery, deepening,<br>and specific surgery-<br>related suggestions for<br>decreased pain and<br>anxiety | 10 min, directly<br>before                                | Beck Anxiety<br>Inventory<br>Hamilton Anxiety<br>Scale  | Pre- and<br>postoperative        | Difference pre-post 4 vs 1, $p < 0.001$<br>5 vs. 0, $p < 0.001$<br>1 vs 3, $p = 0.011$   | None reported  |
| 17 | Slack et al.,<br>2009<br>[46]  | Needle<br>electromyography                          | n = 18,<br>total cohort:<br>65/35.<br>$53.6 \pm 11.7$                                 | $n=8$ , education about EMG total cohort: $65/35$ . $53.6 \pm 11.7$   | Hypnotic induction with $(n = 10)$ and without analgesic suggestion $(n = 8)$ , Barber's 1977 hypnotic procedure, audio recorded                  | 20 min, 45 min<br>prior                                   | VAS pain<br>VAS pain<br>VAS anxiety   | Preoperative<br>Directly after   | $46 \pm 24$ vs. $67 \pm 35, p = 0.049$<br>$33 \pm 25$ vs. $44 \pm 41, p = 0.637$   | None reported  |
| 18 | Schnur et al.,<br>2008<br>[47] | Breast biopsy                                       | n = 49<br>0/100,<br>$46.4 \pm 1.9$  | $n=41, \\ 0/100, \\ 45.0 \pm 2.2, \\ attention-control$   | relaxation-based induction, guided imagery, deepening, and specific surgery-related suggestions for decreased pain, nausea, and distress          | 15 min  | VAS distress<br>Profile of Mood<br>States   | Pre- and<br>postintervention     | lower mean levels of presurgical VAS emotional upset (16.5 vs $38.2$ , $P < 0.0001$ , $d = 0.85$ ), VAS depressed mood (6.6 vs $19.9$ , $P < 0.02$ , $d = 0.67$ ), and SV-POMS anxiety (10.0 vs $5.0$ , $P < 0.0001$ , $d = 0.85$ ); and significantly higher levels for VAS relaxation (75.7 vs $54.2$ , $P < 0.001$ , $d = -0.76$ ) than | None reported  |

(continued on next page)

attention controls.

Table 1 (continued)

|    | ,                              |                                |  |  |  |  |  |                               |  |  |
|----|--------------------------------|--------------------------------|--|--|--|--|--|-------------------------------|--|--|
|    | Author, year Indication        | Indication                     | Number of patients, ratio male/female in percent, average age in years | Control group: number of patients, ratio male/female in percent, average age in years, procedure             | Hypnosis intervention  | Duration and time point of hypnosis intervention | Outcome measure  | Time of outcome<br>assessment | Result   | Adverse<br>reactions<br>related to<br>hypnosis<br>intervention |
| 19 | Saadat et al.,<br>2006<br>[48] | Ambulatory surgical procedures | $n = 26,$ 30/70, $42 \pm 10$   | $n = 26$ , $18/82$ , $39 \pm 10$ , attention-control $n = 24$ , $20/80$ , $43 \pm 10$ , SOC.                 | Ericksonian hypnosis   | 30 min   | State-Trait Anxiety<br>Inventory<br>Heart rate and blood<br>pressure | Pre- and postintervention     | $(31 \pm 8 \text{ vs. } 37 \pm 9 \text{ and } 41 \pm 11; p = 0.008$ ns   | None reported  |
| 70 | Lang et al.,<br>2006<br>[49]   | Breast biopsy                  | n = 78,<br>0/100,<br>49 (range<br>22-84)                               | n = 82,<br>0/100,<br>50 (range 18-82),<br>SOC<br>n = 75,<br>0/100,<br>47 (range 19-86)<br>empathic attention | Self-designed script<br>addressing anxiety,<br>pain and worries. | During procedure                                 | Spielberger State<br>Anxiety<br>Questionnaire<br>(STAI-Y)            | Directly postintervention     | Lower anxiety (SOC: logit slope = $0.18$ , $p < 0.001$ ), empathy group: slope = $-0.04$ , $p = 0.45$ , hypnosis group: slope = $-0.27$ , $p < 0.001$ ) and increase in pain | None reported  |

of care (SOC), placebo, conversational interviews, and other non-hypnotic interventions. The primary outcomes assessed were anxiety, pain; secondary outcomes included physiological parameters such as heart rate and blood pressure. All studies identified through the systematic review that met the inclusion criteria were subsequently included in the meta-analysis.

#### 3.2. Primary outcomes: Anxiety and pain reduction

The pooled analysis demonstrated that hypnosis significantly reduced anxiety and pain compared to control interventions. The standardized mean difference (SMD) for anxiety reduction was -0.43 (95 % CI: -0.58 to -0.28, p < 0.001), indicating a small effect size favoring hypnosis according to the interpretation from Cohen (2013) [21]. For pain reduction, the pooled SMD was -0.35 (95 % CI: -0.50 to -0.20, p < 0.001), also reflecting a small effect size. Heterogeneity among studies was assessed using the  $\rm I^2$  statistic. The  $\rm I^2$  values for anxiety and pain reduction were 45 % and 38 %, respectively, indicating moderate heterogeneity. These findings suggest that hypnosis may effectively alleviate both psychological distress and physical discomfort associated with these procedures.

#### 3.3. Secondary outcomes: Physiological parameters

Significant reductions in physiological parameters were observed in patients undergoing hypnosis. The pooled analysis of heart rate changes showed a mean difference of -5.8 bpm (95 % CI: -7.2 to -4.4, p < 0.001), indicating a reduced heart rate which may suggest a calming effect of hypnosis on cardiac activity. Blood pressure was also significantly reduced, with a mean difference of -6.3 mmHg (95 % CI: -8.5 to -4.1, p < 0.001). These findings support the hypothesis that hypnosis not only reduces subjective pain and anxiety but also modulates physiological stress responses during invasive procedures.

# 3.4. Impact on analgesic use

Several studies reported on the use of analgesics during procedures. In studies where this was assessed, hypnosis significantly reduced the need for pain medication. For example, one study involving atrial flutter ablation reported a significant reduction in morphine use in the hypnosis group (1.3  $\pm$  1.3 mg vs. 3.6  $\pm$  1.8 mg, p< 0.001), highlighting the potential of hypnosis to minimize reliance on pharmacological interventions [22]. Another study on coronary artery bypass grafting noted reduced use of remifentanil (34.4  $\pm$  11.4 mg vs. 50.0  $\pm$  13.6 mg, p= 0.001) and morphine (4.9  $\pm$  3.3 mg vs. 13.6  $\pm$  2.7 mg, p< 0.001) among patients receiving hypnosis [23].

#### 3.5. Adverse reactions

Adverse reactions related to hypnosis were rare and generally mild. Reported side effects included dizziness and sweating in a small number of patients (e.g., 2 out of 50 patients, or 4 %, in one study [24]. No serious adverse effects attributable to hypnosis were reported across the included trials, underscoring the safety of hypnosis as a complementary intervention.

#### 3.6. Subgroup analyses

To further understand the variability in the effectiveness of hypnosis, subgroup analyses were performed based on the following factors: type of hypnosis technique, type of medical procedure, and baseline anxiety levels. These subgroup analyses aimed to identify which factors contributed to the heterogeneity observed in the main results and to provide insights into optimizing hypnosis interventions.

Subgroup analyses based on the type of hypnosis technique revealed significant differences in effect sizes. Studies using virtual reality-

SOC = standard of care, VAS = Visual analog scale, bpm = beats per minute, MAP = mean arterial pressure, ns = not significant

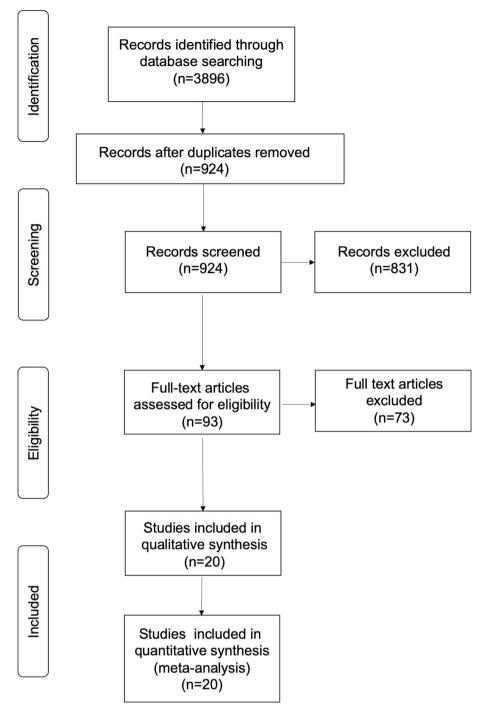


Fig. 1. Flow diagram of study selection.

enhanced hypnosis (e.g., VR masks with guided imagery) showed a substantial reduction in anxiety and pain, with a pooled SMD of -0.58 (95 % CI: -0.75 to -0.41) for anxiety and - 0.50 (95 % CI: -0.67 to -0.33) for pain. These results suggest that the immersive nature of virtual reality may enhance the effectiveness of hypnotic suggestions by fully engaging the patient's attention and reducing environmental stressors. Techniques that involved traditional verbal suggestions, guided imagery, and eye fixation were also effective but showed smaller effect sizes, with an SMD of -0.39 (95 % CI: -0.53 to -0.25) for anxiety and - 0.32 (95 % CI: -0.45 to -0.19) for pain. These methods are commonly used in clinical practice and provide a flexible approach that can be tailored to individual patient needs. Audio-recorded hypnosis sessions had a small effect size with an SMD of -0.25 (95 % CI: -0.39 to

-0.11) for anxiety and -0.21 (95 % CI: -0.34 to -0.08) for pain. This suggests that while audio recordings are convenient, they may be less engaging compared to live or interactive hypnosis sessions.

The effectiveness of hypnosis also varied according to the type of invasive procedure. A moderate effect was observed in studies involving cardiac and vascular interventions (e.g., coronary angiography, cardiac surgery), with an SMD of -0.51 (95 % CI: -0.67 to -0.35) for anxiety and - 0.46 (95 % CI: -0.61 to -0.31) for pain. Hypnosis was less effective in minor surgical procedures (e.g. lumbar puncture, cystoscopy), with an SMD of -0.37 (95 % CI: -0.52 to -0.22) for anxiety and - 0.33 (95 % CI: -0.47 to -0.19) for pain. The effect sizes were also small for diagnostic procedures (e.g. biopsies, endoscopy), with an SMD of -0.28 (95 % CI: -0.42 to -0.14) for anxiety and - 0.26 (95 % CI:

#### -0.40 to -0.12) for pain.

The analysis further examined the impact of baseline anxiety levels on the effectiveness of hypnosis. Patients with higher baseline anxiety levels (measured by pre-intervention scores on tools like the State-Trait Anxiety Inventory) showed greater benefit from hypnosis, with an SMD of -0.54 (95 % CI: -0.70 to -0.38) for anxiety and -0.49 (95 % CI: -0.63 to -0.35) for pain. This suggests that hypnosis is particularly valuable in contexts where psychological distress is prominent. In patients with moderate to low baseline anxiety, the effect sizes were smaller but still significant, with an SMD of -0.30 (95 % CI: -0.44 to -0.16) for anxiety and -0.25 (95 % CI: -0.38 to -0.12) for pain. This subgroup still benefited from hypnosis, but the impact was less pronounced compared to those with higher anxiety levels.

# 3.7. Risk of bias assessment

The risk of bias assessment using the Revised Cochrane Risk of Bias Tool (RoB 2) revealed that the overall risk of bias across the included studies was generally low to moderate. Most studies demonstrated a low risk of bias in key areas such as deviations from intended interventions, missing outcome data, and selection of reported results (Table 2). However, some concerns were noted in the randomization process and measurement of outcomes, particularly in studies with insufficient reporting of randomization methods or reliance on subjective outcome measures, which could introduce potential bias. Despite these concerns, the adherence to intervention protocols was high, and the overall quality of the evidence was deemed reliable.

#### 4. Discussion

This systematic review and meta-analysis provide compelling evidence that hypnosis is an effective and safe intervention for reducing anxiety, pain, and physiological stress responses associated with invasive medical procedures. The pooled results demonstrate that hypnosis offers a moderate but consistent benefit, highlighting its potential as a non-pharmacological adjunct to standard care.

The moderate effect sizes observed for anxiety (SMD = -0.43) and pain (SMD = -0.35) confirm that hypnosis can meaningfully enhance patient experiences during invasive procedures. These results align with previous research that underscores hypnosis as a valuable tool in

modulating both psychological and physiological responses to medical stressors [1]. Notably, the reductions in heart rate and blood pressure observed in this analysis suggest that the effects of hypnosis extend beyond subjective symptom relief to influence autonomic nervous system activity [25], further supporting its role in providing comfort during procedures. The subgroup analyses provide critical insights into how hypnosis can be optimized in clinical practice. The finding that virtual reality-enhanced hypnosis techniques produced the largest reductions in anxiety and pain suggests that immersive, multi-sensory approaches may engage patients more deeply than traditional methods [26]. The virtual reality format not only amplifies the focus on hypnotic suggestions but also distracts patients from the procedural environment, thereby enhancing the overall effect. This points to the importance of further exploring innovative, technology-driven approaches to hypnosis that can be adapted for various clinical settings. Conversely, the smaller effect sizes observed with audio-recorded hypnosis highlight the potential limitations of passive, less interactive formats. While these methods are convenient and easy to implement, the reduced engagement may lessen their impact, particularly in high-stress environments. This suggests that, wherever possible, live or highly interactive hypnosis sessions should be prioritized, especially in procedures associated with elevated patient anxiety. The effectiveness of hypnosis varied notably by the type of medical procedure, with the most significant effects seen in cardiac and vascular interventions. High baseline anxiety levels in these procedures may enhance patients' receptivity to hypnotic suggestions [27]. For less invasive procedures, while the effects were still significant, the smaller effect sizes suggest that the degree of procedural stress may modulate the extent of benefit from hypnosis. These results advocate for a nuanced approach where the decision to employ hypnosis is informed by the specific procedural context and expected anxiety levels. The consistent reduction in analgesic use observed in several studies underscores a critical clinical implication: hypnosis can reduce the need for pharmacological pain management [28], which is particularly valuable in populations where minimizing drug use is essential, such as elderly patients or those with contraindications to certain medications. This not only enhances patient safety but also aligns with broader efforts to reduce opioid reliance in perioperative and procedural care [29]. Moreover, the minimal adverse effects associated with hypnosis across studies reinforce its safety profile, making it an attractive option even for patients who might be at risk of side effects from pharmacological

**Table 2** Risk of bias assessment.

| Study                           | Randomization process | Deviations from intended interventions | Missing outcome data | Measurement of outcome | Selection of reported result | Overall risk of<br>bias |
|---------------------------------|-----------------------|--|----------------------|------------------------|------------------------------|-------------------------|
| Gullo et al. 2023               | Low                   | Low                                    | Low                  | Some concerns          | Low                          | Some concerns           |
| Rougereau et al. 2023           | Some concerns         | Low                                    | Low                  | Low                    | Low                          | Some concerns           |
| Abensur Vuillaume et al. 2022   | Low                   | Low                                    | Some concerns        | Low                    | Low                          | Some concerns           |
| Rousseaux et al. 2022           | Low                   | Low                                    | Low                  | Some concerns          | Low                          | Some concerns           |
| Courtois-Amiot et al.<br>2022   | Low                   | Some concerns                          | Low                  | Low                    | Low                          | Some concerns           |
| Tezcan et al. 2021              | Low                   | Low                                    | Low                  | Low                    | Low                          | Low                     |
| Garcia et al. 2020              | Some concerns         | Low                                    | Low                  | Low                    | Low                          | Some concerns           |
| Fusco et al. 2020               | Low                   | Low                                    | Low                  | Some concerns          | Low                          | Some concerns           |
| Sánchez-Jáuregui et al.<br>2019 | Low                   | Low                                    | Low                  | Some concerns          | Low                          | Some concerns           |
| Lee et al. 2019                 | Low                   | Some concerns                          | Low                  | Low                    | Low                          | Some concerns           |
| Hoslin et al. 2019              | Low                   | Low                                    | Low                  | Low                    | Low                          | Low                     |
| Efsun Ozgunay et al.<br>2019    | Low                   | Low                                    | Some concerns        | Some concerns          | Low                          | Some concerns           |
| Joudi et al. 2016               | Low                   | Low                                    | Low                  | Low                    | Low                          | Low                     |
| Akgul et al. 2016               | Some concerns         | Low                                    | Low                  | Low                    | Low                          | Some concerns           |
| Corman et al. 2016              | Low                   | Low                                    | Low                  | Low                    | Low                          | Low                     |
| Hızlı et al. 2015               | Low                   | Some concerns                          | Low                  | Low                    | Low                          | Some concerns           |
| Slack et al. 2009               | Some concerns         | Low                                    | Low                  | Low                    | Some concerns                | Some concerns           |
| Schnur et al. 2008              | Low                   | Low                                    | Some concerns        | Low                    | Low                          | Some concerns           |
| Saadat et al. 2006              | Some concerns         | Low                                    | Low                  | Some concerns          | Low                          | Some concerns           |
| Lang et al. 2006                | Low                   | Low                                    | Low                  | Low                    | Low                          | Low                     |

sedatives or anxiolytics. The rare incidents of mild symptoms like dizziness and sweating did not detract from the overall safety and tolerability of hypnosis, supporting its broader implementation across diverse patient groups. This finding is consistent with previous reports [30].

To translate these findings into clinical practice, we propose a structured framework for hypnosis in medical settings. First, given that patients with higher baseline anxiety show the greatest benefit, we recommend implementing pre-procedural anxiety screening using validated tools to identify those most likely to respond to hypnosis. Second, virtual reality-enhanced hypnosis should be prioritized as a first-line intervention due to its superior effectiveness. When this is unavailable, live verbal hypnosis should be used instead. Audio recordings, while beneficial, should be considered a supplementary or last-resort option due to their reduced engagement and effectiveness. Third, the impact of hypnosis varies by procedure type, with the greatest benefits observed in cardiac and vascular interventions. Therefore, hospitals should prioritize hypnosis integration in high-stress, high-pain procedures, where its impact is most pronounced. Finally, efforts should be made to share hypnosis protocols, training materials, and virtual reality programs in an open-access format to increase accessibility across diverse healthcare settings. Collaborative initiatives that facilitate crossinstitutional knowledge sharing should be encouraged.

Despite these positive findings, some limitations must be acknowledged. The heterogeneity among studies, as reflected in moderate I<sup>2</sup> values, suggests variability in how hypnosis is implemented and measured across different settings (e.g., verbal suggestions, guided imagery, virtual reality). While the random-effects model used in this analysis accounts for such variability, future research should aim to standardize hypnosis protocols to reduce this heterogeneity. Standardization efforts should focus on core procedural elements (e.g., duration, language structure, and induction techniques), ensuring reproducibility across clinical contexts, while still considering pertinent patient variables. Also, inconsistent use of outcome measurement tools, such as varying pain and anxiety scales, introduces further complexity and potential bias, affecting the reliability of pooled effect sizes. Patientspecific factors also require further exploration to enhance the precision of hypnosis interventions. For instance, gender differences may influence susceptibility to hypnosis, as women may experience greater benefits due to differences in suggestibility, emotional processing, or pain perception [31,32]. Similarly, age differences could play a critical role due to different cognitive processing. Beyond these demographic factors, other elements such as socioeconomic status, education level, and prior exposure to complementary therapies may shape individual receptiveness and outcomes. Additionally, baseline psychological profiles and cultural [31] attitudes towards hypnosis will be crucial in refining patient selection criteria and optimizing intervention effectiveness. Furthermore, the risk of bias assessment revealed some concerns, particularly regarding the randomization process measurement of subjective outcomes, which may influence the reported effect sizes. Another area ripe for exploration is the long-term impact of hypnosis on post-procedural recovery and overall patient outcomes. While this review focused on immediate effects, understanding whether the benefits of hypnosis extend into the postoperative period or influence broader recovery trajectories would provide valuable insights into its role in non-pharmacological patient care.

#### 5. Conclusion

This systematic review and meta-analysis support the integration of hypnosis as a valuable, non-pharmacological intervention in the management of anxiety and pain during invasive medical procedures. Given its demonstrated benefits and low-risk profile, clinical hypnosis should be considered as part of routine standard-of-care to enhance patient experiences and reduce reliance on pharmacological interventions. To facilitate broader clinical adoption, future research should focus on

standardizing hypnosis protocols by defining core procedural elements such as induction techniques, duration, and outcome measures. Establishing validated, evidence-based treatment algorithms will improve methodological consistency, enhance comparability across studies, and ensure reliable implementation in diverse medical settings.

#### CRediT authorship contribution statement

Nike Walter: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Michel Torres Leyva: Writing – review & editing, Project administration, Investigation. Thilo Hinterberger: Writing – review & editing, Validation, Methodology. Markus Rupp: Writing – review & editing, Validation, Supervision. Thomas Loew: Writing – review & editing, Validation, Supervision, Conceptualization. Adolfo Lambert-Delgado: Writing – review & editing, Methodology, Conceptualization. Alberto Erconvaldo Cobián Mena: Writing – review & editing, Validation, Conceptualization.

#### **Declaration of competing interest**

The authors have no conflict of interest to disclose.

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#### Appendix A. Supplementary data

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