

Review Article

Hypnosis for Procedure-Related Pain and Distress in Pediatric Cancer Patients: A Systematic Review of Effectiveness and Methodology Related to Hypnosis Interventions

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Abstract

The aim of this study was to systematically review and critically appraise the evidence on the effectiveness of hypnosis for procedure-related pain and distress in pediatric cancer patients. A comprehensive search of major biomedical and specialist complementary and alternative medicine databases was conducted. Citations were included from the databases' inception to March 2005. Efforts were made to identify unpublished and ongoing research. Controlled trials were appraised using predefined criteria. Clinical commentaries were obtained for each study. Seven randomized controlled clinical trials and one controlled clinical trial were found. Studies report positive results, including statistically significant reductions in pain and anxiety/distress, but a number of methodological limitations were identified. Systematic searching and appraisal has demonstrated that hypnosis has potential as a clinically valuable intervention for procedure-related pain and distress in pediatric cancer patients. Further research into the effectiveness and acceptability of hypnosis for pediatric cancer patients is recommended. J Pain Symptom Manage 2006;31:70–84. © 2006 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Key Words

Hypnosis, pediatric nursing, cancer, pain, anxiety, lumbar puncture, bone marrow aspiration, systematic review

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Introduction

Despite advances in anesthesia and developments in the management of cancer-related procedures, children with cancer (and their parents) regard procedure-related pain from interventions such as lumbar punctures (LPs) or bone marrow aspirations (BMAs) as one of the most difficult and distressing aspects of cancer.^{1,2} Evidence suggests that repetition

of such procedures does not desensitize the child to the distress. Furthermore, distress is known to continue in some patients for years after the completion of anticancer treatment.^{3,4}

Pain is a complex and multifaceted experience. A comprehensive assessment of pain requires variables such as cognitions, behaviors, emotions, physiological reactions, and context to be evaluated and addressed adequately.^{5(p23)} Conventional management of painful and invasive cancer-related procedures in children varies worldwide. In the United Kingdom, for example, the National Institute for Clinical Excellence (NICE) draft *Service Guidelines for Improving Outcomes in Children and Young People with Cancer* emphasize the need for regular painful procedures such as LP and bone marrow biopsy; they highlight the importance of effective pain management for young cancer patients, emphasizing that most children require general anesthesia (points 255–277).⁶ The NICE guidelines acknowledge the role imagination can play in a child's ability to cope with painful procedures by recommending that children in hospital have daily access to play specialists or activity coordinators to assist in preparation for painful procedures. Furthermore, access to formal psychology support and techniques such as relaxation and visualization should be available (point 280).⁶

Health care professionals can play a vital role in improving pediatric procedure-related pain and distress by incorporating psychological interventions alongside standard care. However, an understanding of such interventions, and their evidence for effectiveness, is required to determine the extent to which they can be incorporated into clinical practice. Such evidence can be found by systematically reviewing the literature. For example, a Cochrane systematic review of psychological interventions for needle-related procedural pain and distress in children and adolescents is presently underway.⁷ In addition, there is a planned Cochrane review of the use of nonpharmacological interventions for preparing children and adolescents for hospital care.⁸ Psychological interventions for procedure-related pain and distress are thus placed firmly on the agenda for both practice guidelines and in research.

Hypnosis is one such intervention that has been proposed for use in preparing the child

for procedures including those done under a general anesthetic,⁹ and for incorporation into the management of anticipatory anxiety/distress that surrounds the experience of cancer-related procedures. An independent panel from The National Institutes of Health concluded that there was strong evidence for the use of hypnosis in alleviating chronic pain associated with cancer.¹⁰ A number of published systematic reviews point to the benefits of hypnosis in acute and chronic pain and cancer pain.^{11–14} However, the mechanisms for how hypnosis works are not entirely understood. Hypnosis is a procedure where one person (the subject) is guided by another (the hypnoterapist) to respond to suggestions for changes in subjective experience, such as perception, sensation, emotion, thought, or behavior. Inducing hypnosis can be informal, for example, inviting a subject to listen to or participate in a story or fantasy, or formal, such as inviting the subject to fix their gaze while being given suggestions. Hypnotic induction may also include progressive muscle relaxation (PMR). Hypnosis can be used in a variety of ways to (1) reduce anticipatory stress, (2) develop coping strategies, and (3) block or manipulate the experience of pain. The literature suggests that hypnosis can be tailored to the individual needs, interests, and developmental level of the child.¹⁵ If the subject responds to hypnotic suggestions, it is generally inferred that hypnosis has been induced.¹⁶ In clinical practice, hypnotic suggestion can be tailored to the individual child, incorporating their interests, and using appropriate language for their age. For example, the direct hypnotic suggestion used for a young child undergoing an LP might be

“We will do some strong magic now ... first you have to make your low back go to sleep for a few minutes ... I'll show you how to do it ... I'll just put my hand on your back and help it become sleepy and numb ... soft and sleepy.”¹⁷

Children can be taught self-hypnosis because this has the potential to facilitate self-management of symptoms, thus providing a sense of self-efficacy and mastery over pain and distress. Active participation in one's own care has been shown to have an additional beneficial therapeutic effect in pediatric cancer patients.¹⁸

Hypnotic ability is a trait that remains constant over time,¹⁹ and may be partly genetically determined.²⁰ However, there is evidence that response expectancy and motivation²¹ enhance hypnotic effect. There are various validated scales that measure hypnotic ability and correlate strongly with one another. The Stanford Scale of Hypnotic Susceptibility, Form C, developed by Weitzenhoffer and Hilgard,^{22,23} has become the “gold standard” research tool. However, it is time-consuming and therefore not practical to use in the clinical setting. The shorter Stanford Clinical Scale for Adults and the Stanford Clinical Scale for Children were designed for clinical application.^{24,25} Other validated scales in clinical use include the Children’s Hypnotic Susceptibility Scale,²⁶ the Hypnotic Induction Profile,²⁷ and the Creative Imagination Scale.²⁸ This last scale is quick to administer, requires no induction, and assesses sensory imagination.

There is significant overlap in the hypnosis literature with relaxation techniques, in particular PMR, which also includes elements of ‘induction’ and ‘suggestion.’ Furthermore, research suggests that patients may respond differently to the same intervention depending on what the intervention is called.²⁹

A recently published systematic review into the efficacy of hypnosis in the reduction of procedural pain and distress in children with cancer³⁰ concluded that evidence to date is not robust enough to recommend hypnosis in best-practice guidelines for procedural pain in pediatric cancer management. However, the authors suggested that larger-scale, appropriately controlled trials were justified.

This review suffers from certain limitations. In particular, although the reviewers critically appraised study design, they made no comment on the relevance of outcome measures from a clinical perspective. Furthermore, the review includes a number of uncontrolled studies that may lead to bias in interpreting the results, a factor the authors themselves recognize. A recently conducted randomized controlled trial has been published since the publication of this review.

Aim

This review evaluates the evidence, from controlled clinical trials, for effectiveness of

hypnosis for procedure-related pain and distress in pediatric cancer patients. The methodological quality of studies was appraised, and gaps in the evidence were highlighted. The potential value of hypnosis for clinical practice with pediatric patients is discussed together with suggestions for future research.

Search and Appraisal Methods

Systematic searches of major biomedical, nursing, and specialist complementary and alternative medicine (CAM) databases—MEDLINE, EMBASE, AMED, CISCOP, CINAHL, PsycINFO, and Cochrane Library—were carried out. A search of specialist resources included Cochrane Complementary Field Registry and other Cochrane Group Registries. Search strategies were developed to accommodate the different indexing approaches used by the databases.³¹

Search Terms

Terms for cancer were based primarily on those used by the Cochrane Cancer Network. The basic search terms used are as follows:

neoplasms (exp) or neoplas* or tumor* or tumour* or melanoma* or cancer* or malignan* or leukemia* or leukaemia* or carcin* or metastas* or sarcoma* or antineoplastic agents (exp) or chemotherapy or palliative care (exp) or palliative treatment (exp) or palliative therapy (exp) or terminal care (exp) and hypnosis or hypnosis (exp) or hypnotiz* or hypnotis* or hypnotherapy or hypnotizability or hypnotisability or hypnotic susceptibility or hypnotic-susceptibility (exp) or suggestability (exp) or autosuggestion or autosuggestion (exp) or suggestion (exp) or autohypnosis (exp) or self-hypnosis or posthypnotic or posthypnotic suggestions or posthypnotic-suggestions (exp) or autogenic or autogenic-training (exp).

Efforts were made to identify unpublished and ongoing research using relevant databases, such as the National Research Register (United Kingdom) and clinical trials.gov (United States), together with contacting experts in the field. Reference lists of relevant articles were reviewed to identify further studies.

Filtering

Potential research articles were noted for retrieval and given a preliminary 'study type' categorization according to a flow-chart system developed for this project. The basic study type categories included systematic reviews, randomized controlled trials, controlled clinical trials, uncontrolled studies, case reports, qualitative studies, and surveys. Animal research and basic laboratory-based research were not included in the categorization process. Two reviewers carried out this process independently, notes were compared, and in cases of disagreement, these articles were also retrieved.

Inclusion Criteria

Types of studies. Relevant systematic reviews and controlled clinical trials that included outcome measures for pain were selected. No language restrictions were imposed at the search and filtering stages.

Types of participants. Pediatric patients with a primary diagnosis of cancer undergoing painful and invasive treatment-related procedures (LP, venipuncture, and BMA) were selected.

Types of intervention. Hypnosis was used as a specific intervention (including that directed by self and the therapist).

Types of outcome measures. Patient- and/or observer-reported clinical measures of physical pain or physical pain and anxiety/distress were recorded.

Excluded Studies

The studies that were excluded are shown in Table 1.

Data Collection and Analysis

All relevant studies were appraised, and their methodological quality was assessed. Two researchers independently extracted relevant information using a standardized data extraction and critical appraisal form (DECA form). Differences were resolved by discussion and, if necessary, a third reviewer was involved. Where required, the advice of a statistician was sought. The DECA form was based primarily on a template published by the Centre for Reviews and Dissemination,³² following development and testing by two researchers. The appraisal criteria included details of selection of participants, randomization and blinding, use of intention-to-treat analysis and loss to follow-up, and compliance with treatment.

Clinical Commentaries

A clinician with relevant training and experience in both hypnosis and with cancer patients was asked to comment on each study, focusing on the appropriateness of the intervention,

Table 1

Excluded Studies

Authors	Study Type	Title/Description	Reason for Exclusion
Zeltzer et al. ⁴⁶ 1991	RCT	A randomized, controlled study of behavioral intervention for chemotherapy distress in children with cancer	Chemotherapy treatment not LP/BMA procedure, assessment of distress but not pain
Hilgard and LeBaron ⁴⁷ 1982	UCT	Patients aged 6–19 undergoing BMAs with hypnosis. Hypnotizable but not nonhypnotizable patients reported substantial reductions in self-reported pain relief. The less-hypnotizable patients did not receive symptom relief but reported a reduction in anxiety. Furthermore, females were found to report more pain than males.	No control group
Kellerman et al. ⁴⁸ 1983	UCT	Sixteen adolescent cancer patients undergoing a variety of invasive procedures underwent hypnosis. Patients achieved significant reductions in measures of pain and distress after hypnosis training. Anticipatory anxiety was observed to increase prior to hypnotic treatment. Two patients rejected hypnosis.	No control group

clinical relevance, and practical issues. A semi-structured question format was developed specifically for this. Summaries of these commentaries are provided in Table 2.

Results

One systematic review,³⁰ seven published randomized controlled trials,^{15,17,33–37} and one nonrandomized controlled clinical trial³⁸ were found.

The Evidence

All clinical trials located are presented in Table 2, together with comments on their methodology and clinical relevance. Trials are also further discussed in narrative form to illustrate differences between studies and in an attempt to assist in highlighting the issues to be addressed in future research.

It was not considered appropriate to combine the results of studies due to variation in the population characteristics and in the interventions.

Summary of Each Study

Randomized controlled clinical trials. Liossi and Hatira¹⁵ conducted a four-armed randomized controlled clinical trial (RCT) of 80 pediatric cancer patients (aged 6–16) undergoing LP. Treatment arms included (1) direct hypnosis, (2) indirect hypnosis, (3) therapist attention control, or (4) standard treatment controls. Hypnotic induction included ego strengthening as well as analgesic suggestions and varied according to the child's age, interests, and cognitive/social development. Patients who underwent hypnosis reported less anxiety and pain than control groups. Direct and indirect forms of hypnosis were shown to be equally effective, and level of hypnotizability was significantly associated with treatment benefit in the hypnosis groups. The use of self-hypnosis, however, produced less therapeutic benefit. Methodological limitations include nonreporting of the method of randomization and insufficient information on group equivalence preintervention (sex, cancer stage).

Liossi and Hatira¹⁷ reported a three-armed RCT that evaluated the effect of hypnosis (relaxation and imagery, PMR, abbreviated autogenic training, analgesic suggestions) vs.

cognitive behavioral training (progressive relaxation, autogenic training, breathing exercises, cognitive restructuring, and positive affirmations) and standard care controls in 30 pediatric patients undergoing BMA. Patients who received either hypnosis or cognitive behavioral therapy (CBT) reported less pain and pain-related anxiety than either controls or than their own baseline recordings. There were no significant differences reported on therapy efficacy between the hypnosis and CBT group, however, children in the CBT group reported more self-reported anxiety and observed distress than those in the hypnosis group. Level of hypnotizability was correlated with level of effect in the hypnosis group. Interrater reliability checks for procedural distress strengthened the findings of this study. Methodological limitations included no reporting of method of randomization and small underpowered samples.

Hawkins et al.³³ randomized 30 pediatric cancer patients who were undergoing LPs to receive either direct or indirect hypnotic suggestions. A statistically significant reduction compared with baseline levels for self- and observer-reported pain was found. No statistically significant differences in outcomes were reported between the two different forms/styles of hypnosis. In the absence of a no-treatment or therapist attention control group, no firm conclusions on efficacy can be made for this study. Further methodological limitations include a small sample size, unknown method of randomization, and duration of therapy sessions.

Smith et al.³⁴ compared the effect of a hypnotic intervention to distraction in 36 children aged 4–8 who were receiving venipuncture or Infusapost access procedures. One parent from each child was trained in either hypnosis (fantasy journey) or distraction (with the use of a toy) techniques, before crossing over to receive training in the other intervention. Results pointed to the significance of hypnotizability for treatment effect with hypnotizable children (numbers of which were unknown) showing significantly lower pain, anxiety, and distress scores in response to hypnosis, as compared to low-hypnotizable children or children in the distraction group. Distraction produced significant positive effects for observer-related distress scores in the low-hypnotizable children. Qualitative data suggest that both

parents and children benefited from taking an active role in symptom management by feeling less helpless. Patients in this study were undergoing different interventions than those in the other studies in this review, and this precludes the extent to which direct comparison between studies is possible. Further, the lack of any no-treatment control and inadequate reporting of study design and results limit the conclusions that can be reached from this study.

Wall and Womack³⁸ report the results of a nonrandomized, controlled clinical trial. Patients received training in either hypnosis or cognitive coping strategies prior to treatment with LP or BMA procedure. Patients were grouped for analysis into younger (5–11) and older (12–18 years) groups. Patients in the hypnosis group showed significant decreases in pain and observer-reported anxiety but not patient-reported anxiety, compared with controls. Correlations of hypnotizability were nonsignificant. This was an underpowered small sample with population heterogeneity of age between groups. Statistical procedures are inadequately reported. Results were not differentiated or compared by age despite stratification preintervention. Baseline characteristics are not adequately reported (for example, treatment cycles, time since diagnosis), thus group equivalence preintervention is unknown.

Kuttner et al.³⁵ conducted a three-armed RCT with 48 pediatric leukemia patients who were undergoing BMAs. There were two intervention groups, one of which included hypnosis and the other behavioral distraction (imaginative involvement). The control group received standard care only. Results showed that the interventions were differentially effective for the younger and older children. In the younger group (aged 3–6), hypnosis provided a significant reduction in pain and anxiety compared to the distraction or control groups at first intervention, whereas the distraction group only showed significant results in pain and anxiety after the second intervention. The authors suggest that coping skills for younger children need to be learnt over one or more sessions before any effect can be observed. By contrast, in the older patients (aged 7–10), both the hypnosis and distraction groups showed significant reductions in observer-rated pain and anxiety as compared to controls. This is a small sample with unknown method of randomization. The

contamination of the control group by the staff's increasing knowledge and adoption of the other two treatments was problematic. Furthermore, nurses were inadequately blinded to group allocation. A lack of pretreatment pain measures and high attrition rate further limit the conclusions that can be reached.

Katz et al.³⁶ report the findings of an RCT involving 36 pediatric patients aged 6–11, who were undergoing BMA. Patients were stratified for analysis by sex (24 males and 8 females) based on previous findings of gender differentiation in outcome.³⁹ Patients were randomized to 20 minutes training in hypnosis and self-hypnosis (active imagery, deep muscle relaxation, imagery, and suggestions for anesthesia and self-mastery) or to nondirected play sessions (to control for therapist time and attention). Children in both the hypnosis group and play group demonstrated significant decreases in self-reported measures of pain and fear from baseline to postintervention BMAs with no major statistical differences between groups. No significant main effects or interactions were found on repeated observer measures. Girls exhibited more distress behavior than boys. Approximately half the children underwent LP procedures after the BMAs. This study had a small sample size and unknown method of randomization, blinding, analysis of loss to follow-up, or compliance.

Zeltzer and LeBaron³⁷ randomized 33 patients (aged 6–17) undergoing BMA or LP to receive either hypnosis (individualized imagery, fantasy, and storytelling) or to a control group (behavioral distraction and deep breathing exercises). Mean pain ratings were significantly higher for BMAs than for LPs. During BMA, pain was reduced to a large extent by hypnosis and to a smaller but significant extent by distraction. Anxiety was significantly reduced by hypnosis but not distraction. During LP, hypnosis but not distraction technique showed a statistically significant reduction in pain. The comparison of pain and anxiety outcomes between patients undergoing BMAs and those undergoing LPs is of clinical interest; nevertheless, this was a small sample with unknown method of randomization. The lack of a no-treatment control group precludes firm conclusions on efficacy because the extent to which results may have been due to therapist attention is unknown.

Table 2
Hypnosis in Pediatric Cancer Patients

Study	Study Design	Sample	Inclusion Criteria	CAM Tx	Control	Outcome Measure(s)	Results	Methodology Comments	Clinical Comments
Lioffi and Hatira ¹⁵ 2003 (Greece)	RCT four-armed trial	<i>n</i> = 80. For each of the four arms, <i>n</i> = 20. Age range 6–16. Sex and cancer stage unknown.	Pediatric patients with leukemia or non-Hodgkin's lymphoma undergoing regular LP.	(1) Direct ^a analgesic hypnotic suggestions and (2) indirect ^b analgesic hypnotic suggestions, each for 45 minutes.	(1) Therapist attention for 45 minutes and (2) standard care only.	Nurse observed pain, anxiety with PBCL. Patients assessed pain and anxiety on a 0–5 scale retrospectively after the procedure. Hypnotizability using a Greek translation of the SHCL for Children.	Patients in both hypnosis groups had significantly less self-reported pain ($P < 0.01$), anxiety ($P < 0.01$), and observer-rated distress ($P < 0.01$) than controls. Self-hypnosis was less effective.	Randomization and concealment of allocation unknown. Small, probably underpowered study. Assessors blinded. All completed but 4.5% declined to participate. Compliance and cointerventions unknown.	Appropriate intervention, control group, reporting of outcomes, and follow-up. The positive findings for both direct and indirect suggestions are clinically useful. The finding that response degraded with self-hypnosis is significant.
Lioffi and Hatira ¹⁷ 1999 (Greece)	RCT three-armed trial	<i>n</i> = 30 (CBT Tx = 10, Hypnosis Tx = 10, Ct = 10). Age range 5–15 years. Sex and cancer stage unknown.	Pediatric leukemia patients scheduled for BMA.	Two 30-minute sessions of hypnosis (PMR, abbreviated A.T., analgesic suggestions) 5 days prior to BMAs plus standard care (lidocaine injection for pain).	Two 30-minute sessions of cognitive behavioral therapy (PMR, abbreviated A.T., cognitive restructuring) 5 days prior to BMAs plus standard care (lidocaine injection for pain).	Nurse-reported distress using the PBCL. Patients retrospectively assessed pain and anxiety on a Faces scale (0–5). Hypnotizability was measured using SHCL for Children.	Self-reported pain and anxiety and observer-reported distress were significantly less in the hypnosis and CBT groups than either controls or than their own baseline recordings. No significant differences were observed between the groups.	Randomization and concealment of allocation unknown. Small underpowered study. Blinding of assessors unknown. Patients not blinded. No refusals or losses to follow-up. Compliance unknown. Cointervention of lidocaine injection.	Appropriate intervention, controls, outcome measures, and reporting of outcome. Adequately reported with sufficient follow-up. Good use of relaxation inductions with a variety of suggestions, including ego strengthening.

(continued)

Table 2
Continued

Study	Study Design	Sample	Inclusion Criteria	CAM Tx	Control	Outcome Measure(s)	Results	Methodology Comments	Clinical Comments
Hawkins et al. ³³ 1998 (Greece)	RCT two-armed trial	$n = 30$, unknown n Tx and Ct. Age range 6–16, 12 males and 18 females. Type and stage of cancer unknown.	Pediatric cancer patients undergoing LPs.	(1) Guided imagery plus direct hypnotic analgesic suggestions, and (2) guided imagery plus indirect hypnotic analgesic suggestions. Five days prior to LPs. Unknown duration of interventions.	No placebo or no-treatment control group.	Observer-reported PBCL during the LP. Patients retrospectively assessed pain and anxiety on a Faces rating scale (0–5). Hypnotizability scores were taken (as above). Qualitative data on patient experiences (reported elsewhere).	Postintervention observer- and patient-reported pain and anxiety showed significant reduction over baseline scores. No significant differences between the different forms of hypnosis.	Randomization, concealment of allocation unknown. Small sample size, no placebo, or no-treatment control group. Unknown blinding of assessors. Patients not blinded. All completed with no refusals or losses to follow-up. Compliance and cointervention unknown. Inadequate reporting of treatment time.	Appropriate intervention, outcome measures, and reporting. The study is of value for gathering evidence of what might be used with this group in practice.
Smith et al. ³⁴ 1996 (US)	RCT two-armed trial	$n = 36$ (randomized to undergo sequences of hypnosis and distraction). Age range 4–8, 19 boys and 17 girls. Cancer stage and time since diagnosis unknown.	Hematological (including nonmalignant blood disorders) and oncology pediatric outpatients receiving venipuncture or Infusapost access.	One parent of each child was taught hypnotic (imagination and induction) techniques for use during procedures. Video and audiotape guidance was also provided.	One parent of each child was taught distraction techniques (with a toy) for use during procedures. Video and audiotape guidance was also provided.	OSBD-R. Self-reported CGRS pain and anxiety. Parent reported pain and anxiety. SHCL for Children. Physiological measure of skin conductance response. Procedures were also videotaped and further qualitative data obtained from parent and child.	Hypnotizable children showed significantly lower observer-rated distress ($P < 0.01$), self-reported pain ($P < 0.01$), and anxiety ($P < 0.01$) scores in response to hypnosis. Distraction showed a significant reduction in observer-related distress for the low-hypnotizable children.	Randomization, concealment of allocation unknown. Small sample size with a lack of any placebo or no-treatment control group. Blinding of nurses may have been inadequate. A 25% attrition due to death. Compliance and cointervention unknown. Insufficient details on study design.	Appropriate hypnotic intervention and control group. A good range of outcome measures. Adequate follow-up time. Direct application to clinical practice. Demonstrates the need to assess hypnotizability prior to procedure.

(continued)

Table 2
Continued

Study	Study Design	Sample	Inclusion Criteria	CAM Tx	Control	Outcome Measure(s)	Results	Methodology Comments	Clinical Comments
Wall and Womack ³⁸ 1989 (US)	CCT two-armed trial	<i>n</i> = 20 Ct Tx = 9, Hyp Tx = 11 recruited by invitation. Grouped by age (older = 12–18 years, younger was 5–11 years). Unknown sex, cancer stage, type, time since diagnosis.	Cancer diagnosis undergoing LP or BMA procedures.	2 × training sessions in hypnosis (relaxation, imagery, and induction) 1 week prior to procedure. An audiotope was provided for the second session. Session or tape duration unknown.	2 × training sessions in coping strategies (choice of distraction techniques) 1 week prior to procedure. An audiotope was also provided for the second session. Session or tape duration unknown.	(1) Self-report anticipatory anxiety, procedural anxiety, and procedural pain by VAS. (2) STAI for older (12+) and younger (9–12) children. (3) The McGill Pain Questionnaire for >12 years. (4) Independently observed procedural pain and anxiety by VAS. (5) Heart rate and peripheral temperature. Hypnotizability rated by arm lift. Postprocedural interview.	A significant reduction was shown in observational (<i>P</i> < 0.009) and self-reported (<i>P</i> < 0.03) pain. Observer- (<i>P</i> < 0.04) but not patient-reported (<i>P</i> < 0.217) procedural anxiety showed a significant improvement. Correlations of hypnotizability were nonsignificant.	Randomization and concealment of allocation unknown. Small underpowered sample size with a lack of any placebo or no-treatment control group. Assessor blinded. All 20 completed. Compliance and cointerventions unknown. Statistical results not differentiated by age.	Insufficient information on hypnotic techniques, ages, or measures of hypnotic susceptibility. Appropriate outcome measures and follow-up duration. The finding of greater effectiveness of hypnosis over conscious distraction methods is of relevance to practice.
Kuttner et al. ³⁵ 1988 (Canada)	RCT three-armed trial	<i>n</i> = 48, Hypnosis Tx = 16, Distraction Tx = 16, Control Tx = 16. Age range 3 years, 4 months to 10 years, 3 months (30 males and 18 females). Stratified by age.	Pediatric cancer patients with lymphoblastic leukemia or acute myeloblastic leukemia undergoing ≥2 BMA.	Hypnosis (imaginative involvement, indirect suggestions, and pain switch technique) was provided during BMAs in addition to a 5–20-minute preparation session and standard medical care.	(1) Distraction (choice of distraction technique including toys) was provided during BMAs in addition to a 5–20-minute preparation session and standard medical care. (2) Standard medical care.	Distress was measured by PBRS-R completed by two observers. Observer-rated pain and anxiety on a 5-point Likert scale. (No pretreatment measure of pain.)	For the younger group, hypnosis provided the greatest pain and anxiety relief. Distraction was effective at the second intervention. For the older group, distraction provided the greatest pain and anxiety relief.	Randomization and concealment of allocation unknown. Small insufficiently powered study. Nurses insufficiently blinded. Thirty completed, 37% lost to follow-up, compliance and cointerventions unknown. Contamination of the control group by nursing staff.	Appropriate intervention, control group, outcomes measures, reporting of outcomes, and follow-up duration. Findings in this very young age group (3–6) are clinically relevant because appropriate analgesic dosage is difficult to gauge.

(continued)

Table 2
Continued

Study	Study Design	Sample	Inclusion Criteria	CAM Tx	Control	Outcome Measure(s)	Results	Methodology Comments	Clinical Comments
Katz et al. ³⁶ 1987 (US)	RCT two-armed trial.	<i>n</i> = 36, Hypnosis Tx = 17, Ct Tx = 19. Age range 6–11 years. Stratified by sex.	Pediatric cancer patients with acute lymphoblastic leukemia, undergoing BMAs. Minimum baseline pain, fear, and observer-reported PBRs-R scores.	A 30-minute training in hypnosis (imagery, induction, deep muscle relaxation, and suggestions) and self-hypnosis prior to and for use during BMAs.	Nondirected play sessions prior to and throughout BMA procedure to control for therapist time and attention.	Observer-rated PBRs-R. Fear and pain self-report on a scale of 7. Faces and graphic rating scale of 0–100 patterned after a thermometer. Nurse rating of anxiety on a 1–5 Likert scale. Rapport and hypnotic response was rated on a 1–5 scale by the therapist.	Children in both hypnosis and play groups demonstrated significant decreases in self-reported measures of pain ($P < 0.001$) and fear ($P < 0.001$) from baseline to postintervention BMAs with no major differences between groups. Patient and observer measures did not configure.	Randomization and concealment of allocation unknown. Small underpowered sample size. Unknown method of blinding for observers. Unknown loss to follow-up or compliance. Approximately half the children underwent LP procedures after the BMAs.	Appropriate intervention, control and outcome measures. Outcomes appropriately reported with adequate follow-up time. Good objectives of suggestions. One can only assume that the suggestions were age-appropriate.
Zeltzer and LeBaron ³⁷ 1982 (US)	RCT two-armed trial	<i>n</i> = 33, Tx = 16, Ct = 17. Age range 6–17, 17 males and 16 females. Patients matched for age and disease category.	Pediatric oncology patients undergoing BMA/LPs.	Hypnosis intervention (individualized imagery, fantasy, and storytelling). Therapist was present during all procedures. Duration unknown.	Instruction in deep breathing and distraction (focus on an object in the room). Encouragement of self-control measures.	Observer ratings of pain and anxiety levels on 1–5 scales. Pain and anxiety were self-rated on 1–5 scales.	For BMAs, observer- and self-reported pain was significantly reduced by hypnosis, ($P < 0.001$) and to a smaller but significant extent by nonhypnotic technique ($P < 0.01$). Anxiety was significantly reduced by hypnosis alone ($P < 0.001$). During LP, only hypnosis significantly reduced pain ($P < 0.001$); anxiety was reduced by hypnosis ($P < 0.001$) and to a smaller extent by nonhypnotic technique ($P < 0.05$).	Randomization and concealment of allocation unknown. A small underpowered sample. Blinding of assessors, unknown. 26% attrition rate due to death or treatment completion; 5% refusals. Unknown handling of missing values. Cointerventions and compliance are unknown. Findings were inadequately reported.	Appropriate intervention and control. Adequate reporting. Distraction can itself be hypnotic, but efforts were made to prevent this. This study is highly relevant as an example of sophisticated, individually tailored imagery and hypnotic approach. The use of a ‘hidden observer’ monitors progress.

PBCL = Procedure Behavior Checklist; PBRs-R = Procedure Behavior Rating Scale-Revised; SHCL = Stanford Hypnotic Clinical Scale for Children; OSBD-R = Observational Scale of Behavioral Distress-Revised; CGRS = Children’s Global Rating Scale (pain/anxiety); STAI = State Trait Anxiety Inventory; A.T. = autogenic training.

^aDirect suggestions included, for example, “imagine injecting a local anesthetic into your back.”

^bIndirect suggestions included metaphors, for example, “imagine the colors of the setting sun ... tranquility is available to you whenever you need it....”

To summarize, hypnosis has been compared with a number of different cognitive-behavioral interventions, with groups receiving nonhypnotic therapist attention, and to standard care controls. Positive results have been observed for hypnosis as compared to therapist attention and no-treatment controls for the reduction of procedure-related pain and distress.¹⁵ Both direct and indirect hypnotic suggestions were shown to have advantage over controls.³³ Where hypnosis has been compared with non-directed play³⁶ or to cognitive distraction or coping skills,^{17,34,35,37,38} results were less consistent with no clear differences in benefit between the interventions.¹⁷ Nevertheless, both intervention arms showed increased symptom reduction beyond controls.^{35,37} Some variation in results was found due to the age of the child³⁵ and the extent of hypnotizability.³⁴ Changing from therapist-directed to self-hypnosis¹⁵ resulted in a diminished therapeutic effect. None of the studies reported adverse effects due to the hypnotherapy.

Discussion

Studies reported in this review suffered from some methodological limitations including small underpowered sample sizes and a lack of reporting of the method of randomization, concealment of allocation, and blinding of assessors. In addition, minor omissions in reporting in some papers included a lack of reporting of sampling and recruitment methods and nonreporting of the reasons for why participants were lost to follow-up and of cointerventions and compliance. Inadequate reporting of the duration, content, and context of the hypnosis session (whether suggestions were age appropriate, session duration, rapport, whether parents were present) in some studies presents a challenge for study replication and comparison between interventions.

Outcome Measures

Outcomes for pain and anxiety included both self- and observer-reported measures, typically on a rating scale. In reviewing outcome measures, Lioffi^{5(p53)} suggests that there is much support for the clinical utility and validity of these rating scales in pediatric patient

groups. Studies also included observations of procedure-related behavioral distress using multidimensional checklists or scales.^{15,17,33,34} However, the differences between patient- and observer-reported outcomes for pain and distress levels in the study by Katz et al.³⁶ highlight the need to include both observer- and patient-reported ratings when measuring levels of pain and distress (McCall, personal communication). Anticipatory anxiety as a specific outcome measure is not frequently measured in the research. However, anecdotal evidence (Lioffi, personal communication) suggests that hypnosis can have a positive effect on anticipatory anxiety prior to pediatric procedures. This suggests the need for future research into the impact of hypnosis on anticipatory anxiety in addition to procedure-related distress.

Hypnotizability

Level of hypnotizability was shown to have some influence on analgesic effect. Level of hypnotizability was measured in some studies^{15,17,33,34} using the Stanford Hypnotic Clinical Scale for Children.²⁵ This is an appropriate and validated measure for children. Other measures of hypnotizability were used, including arm levitation exercise and rating scales.^{36,38} However, the reliability and validity of such measures have not been established for this patient group. Studies that show an association between measures of hypnotizability and response to hypnotic analgesia are described elsewhere,⁴⁰ but this is an area that requires further investigation with this population. Measuring suggestibility is clinically relevant as it may help to identify those who might respond readily to hypnosis and those who may require additional training or support.¹⁴

Age and Sex Differences

Patient samples were stratified for analysis by age^{35,37,38} and by sex.³⁶ Sex of the child has been reported to have an impact on the level of pediatric behavioral distress.^{36,39} For example, Katz et al.³⁶ found that boys tended to do better in the play condition and girls tended to do better with hypnosis. The patient population in the study by Kuttner et al.³⁵ included a very young age group (3–6 years) for whom it may be difficult to gauge levels

of pain control. The positive results from the hypnotic intervention for this age are thus of clinical value. However, Kuttner et al. also found that younger children (3–7 years) were less able to use the techniques on their own than were the older children.

Self-Hypnosis vs. Therapist-Induced Hypnosis

Self-hypnosis rather than therapist-induced hypnosis was evaluated less often as an intervention in pediatric patients. This mode of intervention, once learned, has the potential to facilitate self-management of symptoms and self-mastery. Nevertheless, Lioffi and Hatira¹⁵ found that when pediatric patients switched from therapist-directed to self-hypnosis, the beneficial effects on pain and anxiety diminished. Research into the use of self-hypnosis as analgesia in invasive procedures in adults has been conducted.^{41,42} Further research is required to evaluate the feasibility and effectiveness of self-hypnosis in children (and adolescents) of different ages and with different baseline levels of distress throughout the cancer treatment trajectory. The possibility of a dose-response effect from home practice with an audiotape requires further investigation.¹⁴ Furthermore, studies evaluating self-hypnosis might include ‘booster’ sessions to check on technique and provide motivation to continue to practice.

Hypnosis in Association with Standard Care

One key aspect that studies have not all reported on is standard practice. It is not stated in the papers what hypnosis may be replacing or what interventions hypnosis is being used alongside. Standard practice interventions for cancer-related procedures vary, depending on context and country. As mentioned in the introduction, general anesthetic is recommended as standard practice for pediatric procedure-related cancer pain management in the United Kingdom.⁶ However, it has been suggested that hypnosis can be used as an adjunct to pharmacological interventions for pain control and distress management^{15,33} and in preparation for procedures such as general anesthetic.⁹ Health care practitioners, such as nurses, are well placed to provide such supportive interventions. Wolfe et al.⁴³ conducted a survey on 42 nurses to elicit their

perspectives of stress-reduction techniques for procedure-related pediatric cancer pain. The results suggested that nurses considered themselves knowledgeable and competent in several stress-reduction techniques that can be used during painful procedures (such as deep breathing and distraction). However, they considered themselves less knowledgeable and competent with techniques such as play therapy and hypnosis, which they viewed as highly effective in reducing children’s distress.⁴³

Research Recommendations

Hypnotic interventions use different techniques (induction, relaxation, deepening, cognitive-behavioral distraction, and suggestions). Combined with attention received from the therapist, the hypnotic procedure thus includes both specific and nonspecific effects. To date, meta-analytic research has demonstrated that the addition of hypnosis to cognitive-behavioral therapy produces an increase in therapeutic effect.⁴⁴ It has been suggested that comparative, dismantling, constructive, and process-oriented research strategies are required to examine the efficacy of different therapeutic components, and to identify the most effective component(s) or combination.^{14,45} Such evaluations should consider the efficacy of the relative components for certain patient groups, taking into account factors such as age and hypnotizability at the cognitive-developmental level. The benefit of hypnosis needs to be considered against different psychological therapies, such as relaxation, autogenic training, distraction, and visualization techniques. Such knowledge may facilitate the ability to tailor a clinically effective intervention to the specific needs of the child. Although the studies included in this review suggest that adverse effects of hypnosis are limited, further research should consider the safety and acceptability of this technique when used with children.

In addition to the proposals mentioned above, future research should also consider assessing any misconceptions surrounding the intervention that parents of children might have. This could include their expectations of the treatment, the patient and parent experience of the intervention, and patient preferences (what was and what was not helpful).

This type of research would benefit from the application of qualitative research methodologies.

Conclusions

These studies make a significant contribution to the literature by providing specific hypnotic techniques and a framework for further studies. Furthermore, they report positive results, including statistically significant reductions in pain and anxiety/distress. This suggests that hypnosis has potential as a clinically valuable intervention that could contribute to the management of procedure-related pain and distress in pediatric cancer patients. A number of methodological limitations were identified, and further research into the effectiveness and acceptability of hypnosis for pediatric cancer patients is recommended. The potential for hypnotic interventions to be used as an adjunct to pharmacological techniques,^{15,17} and in preparation for a general anesthetic, requires further investigation. The potential influence of hypnosis on anticipatory anxiety has not been evaluated and would benefit from research studies. Further research into the efficacy, feasibility, and safety of hypnosis for pediatric cancer patients with comparisons of age, developmental, and sex variables is recommended. Such evidence will assist in the formulation of evidence-based practice guidelines for using psychological interventions to prepare children for invasive procedures.

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