Published in final edited form as:
J Vasc Interv Radiol. 2008 June ; 19(6): 897–905. doi:10.1016/j.jvir.2008.01.027.

Beneficial Effects of Hypnosis and Adverse Effects of Empathic Attention during Percutaneous Tumor Treatment: When Being Nice Does Not Suffice

Elvira V. Lang, MD, **Kevin S. Berbaum, PhD**, **Stephen G. Pauker, MD**, **Salomao Faintuch, MD**, **Gloria M. Salazar, MD**, **Susan Lutgendorf, PhD**, **Eleanor Laser, PhD**, **Henrietta Logan, PhD**, and **David Spiegel, MD**
Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA (EVL, SF, GS, EL), New England Tufts Medical Center, Boston, MA (SP), the University of Iowa, Iowa City, IA (KS, SL), Iowa City, and the University of Florida, Gainsville, Fl (HL)

Abstract

Purpose—To determine how hypnosis and empathic attention during percutaneous tumor treatments affect pain, anxiety, drug use, and adverse events.

Methods—For their tumor embolization or radiofrequency ablation 201 patients were randomized to receive standard care, empathic attention with defined behaviors displayed by an additional provider, or self-hypnotic relaxation including the defined empathic attention behaviours. All had local anesthetic and access to intravenous medication. Main outcome measures were: Pain and anxiety, assessed every 15 min by patient self-report; medication use with 50μg fentanyl or 1 mg midazolam = 1 unit; adverse events, defined as occurrences requiring extra medical attention including systolic blood pressure fluctuations >50mm Hg and surpassing 180 mm Hg or falling below 105 mm Hg, vaso-vagal episodes; cardiac events, and respiratory impairment.

Results—Hypnosis patients experienced significantly less pain and anxiety than standard care and empathy patients at several time intervals and received significantly less median drug units (mean 2.00, interquartile range (IQR)1-4) than standard (mean 3.00; IQR 1.5-5.0; p = 0.0147) and empathy group patients (mean 3.50, IQR; 2.0-5.9; p = 0.0026). 31 of 65 (48%) patients in the empathy group had adverse events, significantly more than those in the hypnosis (8/66 (12%); p=0.0001) and standard care groups (18/70 (26%); p=0.0118).

Conclusions—Procedural hypnosis including empathic attention reduces pain, anxiety, and medication use. Conversely, empathic approaches which provide an external focus of attention and do not enhance patients' self-coping can result in more adverse events. These findings should have major implications for the education of procedural personnel.

The material was presented at the 2007 SIR meeting in Seattle

Disclosures: After completion of the study E V Lang established Hypnalgesics LLC to provide training of healthcare providers in procedural hypnosis. The other authors declare no competing interest.

INTRODUCTION

Self-hypnotic relaxation, provided to patients on the procedure table, has been shown to decrease pain, anxiety, drugs use, and adverse events during peripheral vascular and renal interventions (1). We questioned whether these results would also apply to more invasive procedures, such as percutaneous tumor treatments. We designed a prospective randomized trial to test the effects of procedural hypnosis in patients undergoing transcatheter embolizations and radiofrequency ablations. In addition, we were interested in the effect of the attention that patients receive in a trial, particularly in one that assesses the effects of a communicative mind-body intervention. This also responds to the increasing emphasis of organizations overseeing medical education on empathy and competency in interpersonal and communication skills (2,3).

In past studies, patients undergoing interventional procedures benefited to various degrees from structured empathy, which was included as an active control condition (1,4). Therefore, we included in our planned trial an empathic attention control condition to assess its effect on patients' perception and well-being. We felt that this design could help shed more light on the issue of clinical empathy which is subject to various interpretations, (5-8) and which few prospective randomized trials correlate behaviors with patient outcomes.

MATERIALS AND METHODS

Patients

The study was conducted in an urban tertiary medical center with approval of its Human Subjects Review Board. Adult patients referred for percutaneous tumor treatment by transcatheter embolization or radiofrequency ablation who were able and willing to give written informed consent were recruited. Exclusion criteria were bodyweight <55 kg, a score of <26 on the Mini-Mental-State test (9), indication of psychosis or serious mental disease, severe chronic obstructive pulmonary disease, home use of oxygen, intolerance of midazolam and fentanyl, pregnancy, and inability to hear or understand English.

Interventions Overview and Randomization

Methodology was modelled after published trials assessing the effect of self-hypnotic relaxation during invasive medical procedures (1,4). Patients were randomly assigned to receive standard of care, empathic attention, or self-hypnotic relaxation treatment (consisting of empathic attention plus reading of a hypnosis script) while on the procedure table. After consent for the invasive medical procedure, a research assistant obtained consent for participation in this study, performed mental and psychosis screening, and had patients fill out a Spielberger State Trait Anxiety Inventory (10). Random numbers in sealed envelopes determined the sequence of group assignment for consecutive patients. The envelopes were opened just prior to the patient's entry into the procedure room.

We hypothesized that adjunct self-hypnotic relaxation provided on the procedure table would (1) reduce patients' pain, anxiety, and medication use; and (2) reduce the frequency of adverse events.

Tumor Treatment

Tumor embolizations employed standard angiographic technique via a transfemoral approach and superselective catheterization with 3-5 French catheters (11,12). Benign tumors (mostly uterine fibroids) were embolized with 300-700 μn polyvinyl alcohol (Boston Scientific, Natick, MA) or trisacryl gelatin particles (BioSphere Medical, Rockland, MA), hepatic malignancies with doxorubicin (primary tumors) or mitomycin (metastases) in ethiodized oil followed by

gelfoam slurry. Radiofrequency ablation followed published technique (13) using CT guidance,17-gauge RF-electrodes and a 500 KHz monopolar generator capable of producing 200 W (Radionics Inc, Burlington, MA).

All patients received local anesthetic, intravenous (IV) hydration and antimicrobial prophylaxis. Pretreatment for chemoembolization included allopurinol, hydroxyzine, granisetron, and famotidine perorally and 2 mg hydromorphone subcutaneously; patients with carcinoid also received periprocedural IV octreotide. All 89 women with uterine fibroids received 30 mg IV ketorolac just prior to particle delivery; the last 43 also had pre-procedure scopolamine hydrobromide patches.

Interventions

All patients were attended by one or two procedure nurses and technologists, an interventional radiologist and fellow and/or radiology resident. In the Empathy and Hypnosis groups, an additional research assistant sat at the patients' head protected by a mobile transparent lead glass shield hidden behind the radiation tower (or CT gantry) from site of the operators who were working on the patients' opposite extreme.

In both treatment conditions the assistant displayed 8 standardized empathic attentive behaviours specified in the treatment manual and published in abbreviated form (14): matching the patient's verbal preferences, adapting to the patient's nonverbal communication pattern, listening attentively, providing the perception of control ("Let us know at any time what we can do for you"), swiftly responding to patient's requests, encouraging the patient, avoiding negatively-valued language (e.g. "You will feel a burn and a sting") and using emotionally neutral descriptors instead (e.g. "This is the local anesthetic"). In the Hypnosis Group the assistant also read a hypnosis script (4)which invites patients to roll their eyes upwards, close their eyes, breathe deeply, focus on a sensation of floating, and experience a pleasant setting of their choice with all their senses. The text suggested transforming potential discomfort into a sensation of warmth, coolness, or tingling. If needed, a provision in the script guided patients to project their worries and fears onto the left side of an imaginary split screen and find solutions on the right side of the screen. The research assistants coached the patients according to the script and the treatment manual in developing their own imagery and solutions.

The empathic and hypnosis conditions were provided by 6 researchers assistants (one male and two female physicians, 2 female medical students, one premedical student with a psychology background) who had been trained and tested to reliably execute all key behaviors. To enhance fidelity of treatment administration (15) all procedures were videotaped. 57 tapes (28%) were randomly selected and analyzed by 2 other researchers not involved in the cases but who had been trained to assess execution of prescribed and proscribed behaviors with an inter-rater reliability of 0.88. Adherence to the protocol was high. There was no difference in the frequency of and extent to which the research assistants displayed the structured empathic behaviors in the empathy and hypnosis groups.

Hemodynamic and Respiratory Measures

Heart rate, electrocardiogram, respiratory rate, and oxygen saturation were monitored continuously and blood pressure was monitored every 5 minutes by automated clinical equipment and recorded by nursing staff.

Adverse Events and Complications

Adverse events were defined as all occurrences that would attract extra medical attention to restore hemodynamic and cardiorespiratory stability. Patients' vital signs reflect their cardiovascular reactivity and can change based on anxiety levels, pain, sympathetic arousal,

vagal stimulation, effects of sedatives and analgesics, and in response to liberation of the content of hormone active tumors. When blood pressure and heart rate change during a procedure the operator often does not know immediately the cause of the change and the extent to which the change will progress. We therefore chose changes that, in our practice, would cause the operator or nursing staff to take notice and consider treatment, or in the least divert attention from the ongoing procedure. Inclusion required presence of at least one of the following: systolic blood pressure fluctuations >50mm Hg with one value surpassing 180 mm Hg or falling below 105 mm Hg, unless the trend was towards a more normal value from initial hypertension; vaso-vagal episodes; de novo diastolic hypertension >95 mm; cardiac arrhythmia; chest pain; tachycardia >100 beats per minute; and respiratory disturbances. We used as guidance elements of the modified Aldrete score (16), but rather than using percentages of pre-procedure values or absolute limits alone we chose the 50 mm Hg systolic changes only if they either produced hypertensive values in a normotensive person or if they resulted in relative hypotension in a hypertensive individual. For example, a 50% increase in systolic blood pressure from 100 to 150 mm Hg would not be as worrisome as the same rate of increase in a patient with a baseline of 130 mmHg who would reach 185 mm Hg systolic; a 30% decrease in systolic blood pressure from 180 mm Hg to 120 mmHg would be more comforting than a decrease from 150 mm Hg to below 100 mm Hg.

Complications were reported according to the Reporting Standards by the Society for Interventional Radiology (17).

Pain, Anxiety, and Medication

Pain and anxiety were assessed by self-reporting on verbal scales which were previously validated and found reliable for use in this setting (18,19). Every 15 minutes, the researcher asked the patients to rate their comfort between 0 (no pain at all) and 10 (worst pain possible), and their anxiety between 0 (no anxiety at all) and 10 (terrified). When patients indicated discomfort outside the queries, another rating was obtained and the worst score was used as representative for the 15-minute interval.

Patients' intraprocedural use of sedatives and analgesics (beyond the premedication and intraprocedural ketorolac) was assessed in a modified PCA model which had been found applicable in this setting (1): Patients were given a button to press to alert the attending nurse to administer one IV drug unit. Patients had access to a combination of sedatives and analgesics. Drug units were based on the customary standard in the procedure suite and consisted of 0.5 mg midazolam plus 25 μg fentanyl per dose up to 4 times with a lock-out time of 5 min, followed by a lockout time of 15 min. Medication was withheld when the systolic blood pressure fell below 89 mm Hg, oxygen saturation decreased to <93% despite nasal oxygen, the patient developed slurred speech, or was difficult to rouse. Patients received additional medication when they verbally asked for it, became hypertensive or tachycardic (except during a carcinoid crisis), or when distress and movements might have interfered with procedural progress. Rules for overriding the patients' choice of drug use in the PCA model were agreed upon by the procedure personnel before the study and were reviewed on an ongoing basis.

Procedure Time

Procedure time was recorded as the entire time the patient occupied the procedure room.

Blinding

Adverse events were based on recordings from standard hospital electronic equipment and entries on standard hospital procedure flow sheets by the nursing staff within their routine duties. Occurrence of adverse events was based on the nursing notes without knowledge of the group attribution and using the objective parameters outlined above. Although the operator

was separated by the research assistant through the imaging tower or CT gantry and thus not in easy auditory range of the interactions between research assistant and patient, complete blinding was not possible.

Statistical Analysis

Sample size analyses for the present study relied on estimates of the time courses of pain and anxiety ratings from a prior study with the same design and measures (1). For a linear mixed model using smoothed correlations for 8 successive bands in a within-subjects correlation matrix, calculations with the RMASS2 program (20), a compound symmetry *rho* = 0.70, one-sided *alpha* = 0.05, power = 0.80, attrition data estimates from the previous study, and *ES* = 0.71, 94 subjects were required within a treatment condition (282 overall). When a high adverse event rate in the empathy group became evident at the semi-annual Data Safety Monitoring Board meeting, the study was halted after enrollment of 201 patients.

With reduced patient numbers and the inability to convert pain and anxiety ratings into normally distributed data sets, nonparametric Mann-Whitney Rank Sum tests were used. Data were analyzed on an intent-to-treat bases. While the measurements at different time points can be considered to be interdependent, comparisons among standard vs. empathy, standard vs. hypnosis, and empathy vs. hypnosis treatment were considered to be independent of each other and we therefore used the Bonferroni corrections to place the significance level at 0.05:3=0.0167 in two-tailed tests. The same testing was applied to the analysis of medication use and procedure time. Medians and interquartile ranges (IQR), defining values between the 25^{th} and 75^{th} percentiles, were given to illustrate central tendencies for these variables. Frequency of adverse procedural events was compared among standard vs. empathy, standard vs. hypnosis, and empathy vs. hypnosis treatment by two-tailed Fisher Exact Test at a significance level of 0.05:3=0.0167.

RESULTS

Between September 2004 and June 2006, 232 consecutive patients were assessed for eligibility. Ten were unable to understand English. 20 refused to participate in this randomized study, and one failed psychosis testing. The remaining 201 patients were randomized: 70 were allocated to and received standard of care intervention; 65 were allocated to and received empathic attention; and 66 were allocated to and received guidance in self-hypnotic relaxation. Table 1 summarizes the patient characteristics, which were relatively homogenous among groups.

Figs. 1a and 1b depict the time course of the median pain and anxiety ratings. Table 2 provides the data spread, p-values, and patients remaining for each procedure interval. Anxiety decreased significantly in the hypnosis group compared to the standard group in the first 15-30 min. By 30-45 min anxiety in the hypnosis group was significantly decreased as compared to the standard and also empathy group. Pain was significantly less for hypnosis than standard and empathy patients in the 15-30 and 30-45 min intervals. In the 75-90 min interval, when effects of tissue ischemia and cell death were expected to begin, and also at 120-135 min, hypnosis patients experienced significantly less pain and anxiety than empathy patients. As best seen on Fig. 1 b, patients in the standard group had varying anxiety and pain experiences which overall did not differ significantly from those in the empathy group.

Hypnosis patients received significantly less medication (mean 2.00, IQR 1-4) than standard group patients (mean 3.00; IQR 1.5-5.0; p = 0.0147) and empathy group patients (mean 3.50, IQR; 2.0-5.9; p = 0.0026) who did not differ from each other (p=0.4505).

When the trial was halted, 31 of 65 (48%) patients in the empathy group had experienced adverse events at a significantly higher frequency than those in the hypnosis (8/66 (12%);

p=0.0001) and standard group (18/70 (26%); p=0.0118). The difference between standard and hypnosis groups showed a trend but was not significant (p=0.0514). In the empathy group there were not only more patients who had adverse events, but those who had them also tended to experience more often more than one adverse occurrence (Table 3). Delayed complications are shown in Table 4. Small event numbers in the individual complication subcategories did not provide sufficient power to enable meaningful comparisons among the groups.

Median procedure duration (IQR) was 110.0 min (IQR 90-151min) for the standard group, 120.0 (IQR 83-140 min) for the empathy group, and 110.0 (IQR 75-145 min) for the hypnosis group. The differences were not significant (p-values between 0.7728 and 0.9109).

DISCUSSION

Hypnosis patients had less pain, anxiety, and medication use than patients receiving standard care treatment. This is consistent with previous trials of invasive medical procedures (1,4, 21-23), although the procedures in this study were more invasive by induction of tissue death, and patients were aware of overall greater treatment risks. Surprisingly, findings in the empathy group differed markedly from prior studies (1,4). A strikingly high adverse event rate (31/65; 48%) significantly exceeded that under hypnosis (8/66; 12%) and standard care (18/70; 26%) and ultimately prompted halting this trial. We were able to treat all the occurrences successfully, and small patient numbers in consideration of the low delayed major complication rates do not permit a statistically meaningful conclusion about the long-term impact. One should, however, not underestimate the stress such procedural adverse events place on team and patients. At the time of their occurrence it is not clear whether these events are reversible or portend further untoward sequelae. We therefore chose to err on the side of patients' safety.

Hypnosis has been shown to reduce cardiac sympathetic activity and myocardial ischemia during percutaneous transluminal angioplasty (24) and to improve the heart rate variability profile (25,26), a quantitative measure of changes in intervals of heart beats associated with autonomic function and predictive of cardiovascular risk (27). Trance can occur spontaneously without formal induction, particularly under conditions of stress (28). Patients in the hypnosis group - and possibly some in the standard group, who might have experienced spontaneous hypnosis - may have benefited from such improved autonomic function and thus may have escaped excessive adverse events. Conversely, patients in the empathic attention condition may have been less able to engage their internal coping skills due to the external focus of attention i.e., the sympathizing personnel, thus resulting in poorer autonomic function and higher rates of adverse events. The higher medication use in the empathy group, in contrast to a prior vascular/renal intervention trial (1), may be partly explained by the provision in the protocol that patients who become hypertensive or tachycardic could receive nurse-administered medication without patient request. It is also possible that the higher medication is an expression of the greater reliance on external provision of comfort. That there was no significant difference in room time among groups is likely due to the rate-limiting slowness by which embolization agents can be infused and radiofrequency-necrosis can be induced.

Percutaneous tumor treatments are prone to induce patient distress. Perceiving others in distress produces an affective response, which is oriented to decrease distress to the observer as well as to the suffering person, and elicits a behavioural response, which may be targeted towards providing comfort and reassurance or withdrawl (29). This affective response to the perception of others' pain can be documented on functional MRI and is the higher in intensity the higher the observer scores on empathy scales (30). Higher scores on empathy scales however do not necessarily translate in appropriate clinical behaviour. A study in the postoperative acute care setting reports that nurses who scored higher on such empathy scales, but did not have advanced education in patient interactions, did not provide better pain management for their patients

(31). Well-meant sympathizing comments by caregivers can even produce nocebo effects if wording is not chosen carefully (32,33). In a setting where physicians and nurses are aware of the procedural risks and may have witnessed serious complications and even death on the procedure table, one should not underestimate the fears these individuals bring with them into the procedure room. During review of the videotapes we noted often nervous laughter and attempts at lightening the atmosphere with gentle jokes when patients were first brought into the room. One may speculate that seeing the expression of a patient becoming more relaxed while entering trance may potentially also calm the procedure team.

In the standard care condition, nurses left patients mainly on their own once the procedure started, checked on their well-being from time to time, when called by the patient, or at critical parts of the procedure. In the empathy condition, nurses engaged to a greater extent with the patient and the empathic care provider. There were more frequent interactions of a conversational nature. These conversations followed patterns of social interactions; e.g. when patients mentioned topics such as travel, careers, or encounters with the health care system, nurses expressed understanding and sympathy by contributing their own experiences. Rather than being a pleasant distraction, such discussions may have been experienced as disinterest on the part of the caregiver in the patient's distress. It is also possible that the responsive stance activity in the empathy condition served to further focus subjects' attention on their reported distress without giving them a means of controlling that distress, thereby compounding it. Conversely, in the hypnosis group, topics the patient mentioned were used by the researchers to structure desirable imagery, and, if they hinted at distressing emotional content, were further explored and addressed according to the provisions of the script and training manual. The focus was on helping patients help themselves. Thus the researcher displaying empathic attention skills did not remain an external focus of coping as in the empathy only group, but enabled patients to mobilize their own internal resources and engage in self-hypnosis.

There are various interpretations of empathy (5-8). In a review, Irving et al showed how the construct of empathy is surrounded by "ambiguity and conceptual confusion" and how this complicates its study and application in the health setting (7). A patient's experience may be far from that of the caregiver, and emotional understanding requires careful listening on the part of the observer so that the observer's response can match the patient's affective state (34). While nurses in our study expressed great sympathy the results seem to support that trying to be "nice" does not suffice. Ideally, a positive feedback is set up from which the observer can identify the patient's feelings, concerns or quandaries and reflect that back in an appropriate empathic response. This however requires considerable interpersonal skill training.

The study has limitations. We halted the trial because of a high adverse event rate in the empathy group. Analyses of the original planned primary outcomes (pain, anxiety, drug use, and adverse events) could not be performed at the power level planned and statistical analyses were adapted to the lower patient numbers. Total blinding of the operators was not achieved since the voice level in the procedure room and whole atmosphere typically calmed considerably after induction of hypnosis. Pain and anxiety data may have been biased since the individuals structuring empathy and hypnosis obtained them, but these demand characteristics should then have affected patients' ratings in both conditions similarly. Moreover, the main finding of the study, the difference in adverse event rates, was based on objective hemodynamic and respiratory data obtained from automated machines.

This study was able to show beneficial effects of analgesic and anxiolytic hypnotic techniques employing hypnosis in conjunction with empathic attention during invasive tumor treatment and the adverse effects empathy alone without appropriate behavioral responses can elicit. Other treatments with a lower probability of hemodynamic and cardiorespiratory disturbances would have required much larger patient numbers to provide sufficient power for a meaningful

comparison among groups. For example, in a trial with 236 women undergoing large core breast biopsy with local anesthesia only, there were one vasovagal episode in the standard care group, two in the empathy group, and none in the hypnosis group (4). Less invasive procedures have lower odds of adverse events overall, but they are performed more commonly, and in the aggregate, potential adverse effect of an incomplete empathic approach can affect large numbers of patients and caregivers. It is important for caregivers to be aware of the effect of their behavior on patient outcomes not only in psychosocial but also hemodynamic terms. This will require considerable efforts in promoting awareness and training. It would appear that non-specific support without providing means of managing acute pain and anxiety may do more harm than good.

Acknowledgments

This work was supported by the National Institutes of Health, National Center for Complementary and Alternative Medicine RO1-AT-0002-07 and 1K24- AT- 01074. The funding agency was not involved in the design and conduct of the study, data analysis, and approval of the manuscript. The content is solely the responsibility of the authors and does not necessarily reflect the official views of the funding agency. We greatly appreciate the expert research assistance from Olga Hatsiopoulou, MD, Noami Halsey, BS, Tony Wong, BS, Verena Stinshoff, MD, Christine Schupp, MD, Eva Kettenmann, and Nicole Flory, PhD. The persons acknowledged were salaried by the Institution and contributed within their employment.

REFERENCES

1. Lang EV, Benotsch EG, Fick LJ, Lutgendorf S, Berbaum ML, Berbaum KS, et al. Adjunctive non-pharmacologic analgesia for invasive medical procedures: a randomized trial. Lancet 2000;355:1486–1490. [PubMed: 10801169]
2. Accreditation Council for Graduate Medical Education. Outcome Project. ACGME; Chicago, IL: 2001.
3. Stepien KA, Baernstein A. Educating for empathy. J Gen Intern Med 2006;21:524–530. [PubMed: 16704404]
4. Lang EV, Berbaum K, Faintuch S, Hatsiopoulou O, Halsey N, Li X, et al. Adjunctive self-hypnotic relaxation for outpatient medical procedures: A prospective randomized trial with women undergoing large core breast biopsy. Pain 2006;126:155–164. [PubMed: 16959427]
5. Banja JD. Empathy in the physician's pain practice: Benefits, barriers, and recommendations. Pain Med 2006;7:265–275. [PubMed: 16712628]
6. Halpern J. What is clinical empathy? J Gen Intern Med 2003;18:670–674. [PubMed: 12911651]
7. Irving P, Dickson D. Empathy: towards a conectual framework for health professionals'Int J Health Care Qual Assurance. Int H Health care Qual Assurance 2004;17:212–220.
8. Suchman A, Markakis K, Beckman HB, Frankel R. A model of empathic attention in the medical interview. JAMA 1997;277:678–682. [PubMed: 9039890]
9. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. J Psychiatric Res 1975;12:189–198.
10. Spielberger, C. Manual for the state-trait anxiety inventory STAI (form Y). Consulting Psychologists; Palo Alto: 1983.
11. Pron G, Bennett J, Common A, Wall J, Asch M, Sniderman K, et al. The Ontario Fibroid Embolization Trial. Part 2. Uterine fibroid reduction and symptom reflief after uterine artery embolization for fibroids. Fertility Sterility 2003;79:120–127.
12. Stuart K, Stokes K, Jenkins R, Trey C, Clouse M. Treatment of hepatocellular carcinoma using doxorubicin/ethiodized oil/gelatin powder chemoembolization. Cancer 1993;72:3202–3209. [PubMed: 7694787]
13. Livragi T, Solbiati L, Meloni F, Ierace T, N GS, Gazelle GS. Percutaneous radiofrequency ablation of liver metastases in potential candidates for resection: the "test-of-time approach". Cancer 2003;97:3027–3035. [PubMed: 12784338]
14. Lang EV, Lutgendorf S, Logan H, Benotsch E, Laser E, Spiegel D. Nonpharmacologic analgesia and anxiolysis for interventional radiological procedures. Sem Intervent Radiol 1999;16:113–123.

15. Moncher FJ, Prinz RJ. Treatment fidelity in outcome studies. Clin Psychol Rev 1991;11:247–266.
16. Aldrete JA. The post-anethesia recovery score revisited. J Clin Anesth 1995;7:89–91. [PubMed: 7772368]
17. Standards of Practice Committee of the Society of Cardiovascular and Interventional Radiology. Standards for Interventional Radiology. JVIR 1991;2:59–65. [PubMed: 1839231]
18. Benotsch E, Lutgendorf SK, Watson DW, Fick LJ, Lang EV. Rapid anxiety assessment in medical patients: evidence for the validity of verbal anxiety ratings. Ann Behav Med 2000;22:199–203. [PubMed: 11126464]
19. Murphy D, McDonald A, Power A, Unwin A, MacSullivan R. Measurement of pain: A comparison of the visual analogue with a nonvisual analogue scale. J Clin Pain 1988;3:197–199.
20. Hedeker D, Gibbons RD, Waternaux C. Sample size estimation for longitudinal designs with attrition: Comparing time-related contrasts between two groups. J Edu Behav Stat 1999;24:70–93.
21. Faymonville ME, Mambourg PH, Joris J, Vrijens B, Fissette J, Albert A, et al. Psychological approaches during conscious sedation. Hypnosis versus stress reducing strategies: a prospective randomized study. Pain 1997;73:361–367. [PubMed: 9469526]
22. Faymonville ME, Meurisse M, Fissette J. Hypnosedation: a valuable alternative to traditional anaesthetic techniques. Acta Chir Belg 1999;99:141–146. [PubMed: 10499382]
23. Montgomery GH, David D, Winkel G, Silverstein JH, Bovberg DH. The effectiveness of adjunctive hypnosis with surgical patients: A meta-analysis. Anesth Analg 2002;94:1639–1645. [PubMed: 12032044]
24. Bagline R, Sesana M, Capuano C, Gnecchi-Ruscone T, Ugo L, Danzi G. Effect of hypnotic sedation during percutaneous transluminal coronary angioplasty on myocardial ischemia and cardiac sympathetic drive. Am J Cardiol 2004;93:1035–1038. [PubMed: 15081451]
25. DeBenedittis G, Cigada M, Bianchi A. Autonomic changes during hypnosis: A heart rate variability power spectrum analysis as a marker of sympathico-vagal balance. Int J Clin Exp Hyp 1994;42:140–152.
26. Hippel CV, Hole G, Kaschka WP. Autonomic profile under hypnosis as assessed by heart rate variability and spectral analysis. Pharmacopsychiatry 2001;34:11–113.
27. Stein P, Domitrovich PP, Hui N, Rautaharju P, Gottdiener J. Sometimes higher heart rate variablity is not better heart rate variability: Results of graphical and nonlinear analyses. J Cardiovasc Electrophysiol 2005;16:1–6.
28. Barabasz AF. Wither spontaneous hypnosis: A critical issue for practioners and researchers. Am J Clin Hypn 2005;48:2–3.
29. Goubert L, Craig KD, Vervoort T, Morley S, Sullivan MJL, de Williams ACC, et al. Facing others in pain: the effect of empathy. Pain 2005;118:285–288. [PubMed: 16289804]
30. Singer T, Seymour B, O'Dohert J, Kaube H, Dlan RJ, Frith CD. Empathy for pain involves the affective but not sensory components of pain. Science 2004;303:1157–1162. [PubMed: 14976305]
31. Watt-Watson J, Garfinkel P, Gallop R, Stevens B, Streiner D. The impact of nurses' empathic responses on patients' pain management in acute care. Nurs Res 2000;49:191–200. [PubMed: 10929690]
32. Lang EV, Hatsiopoulou O, Koch T, Lutgendorf S, E K, Logan H, et al. Can words hurt ? Patient-provider interactions during invasive medical procedures. Pain 2005;114:303–309. [PubMed: 15733657]
33. Spiegel H. Nocebo: the power of suggestibility. Prevent Med 1997;26:616–621.
34. Coulehan JL, Platt FW, Egener B, Frankel R, Lin CT, Lown B, et al. "Let me see if I have this right..." Words that help build empathy. Ann Intern Med 2001;135:221–227. [PubMed: 11487497]

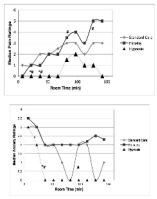

Fig. 1a and b.

Median Pain Ratings (a) and Median Anxiety Ratings (b) Source data from Table 2 which contains the interquartile ranges and patients remaining at each interval. * indicates a significant difference between hypnosis and standard treatment, and # indicates a significant difference between empathy and hypnosis treatment. Significance level 0.0167. Ischemic changes are anticipated around 50 min of room time.

Table 1

Patient Characteristics * median (range)

Characteristic	Standard (n=70)	Empathy (n=65)	Hypnosis (n=66)
Age – years*	50.5 (29-79)	51(27-88)	48 (33-75)
Weight – kg*	68 (48-140)	69 (45-112)	69 (42-143)
Male	31 (44.3%)	22 (33.8%)	21 (31.8%)
Female	39 (55.7%)	43 (66.2%)	45 (68.2%)
Ethnicity			
Non-Hispanic/Latino	66 (94.3%)	62 (95.4%)	64 (97.0%)
Hispanic/Latino	4 (5.7%)	2 (3.1%)	2 (3.0%)
Unknown	0 (0%)	1 (1.5%)	0 (0%)
Race			
White	51 (72.9%)	48 (73.9%)	49 (74.2%)
Black/ African American	16 (22.9%)	14 (21.5%)	13 (19.7%)
Asian/ Asian American	3 (43%)	3 (4.6%)	2 (3.0%)
Multiple	0 (0.0%)	0 (0.0%)	1 (1.5%)
Unknown	0 (0.0%)	0 (0.0%)	1 (1.5%)
Marital Status			
Single	22 (31.4%)	15 (23.1%)	13 (19.7%)
Married	37 (52.9%)	41 (63.1%)	38 (57.6%)
Widowed	3 (4.3%)	5 (7.7%)	3 (4.5%)
Divorced	5 (7.1%)	2 (3.1%)	7 (10.6%)
Other	2 (2.9%)	1 (1.5%)	3 (4.5%)
Unknown	1 (1.4%)	1 (1.5%)	2 (3.0%)
Spielberger State Anxiety*	21.5 (0-61)	23 (10-65)	21.5 (10-62)
Prior Angiographic Procedure			
First Procedure	60 (85.7%)	57 (87.7%)	59 (89.4%)
Prior Procedure	10 (14.3%)	8 (12.3%)	7 (10.6%)
Tumor Type/Treatment			
Hepatic malignancy, total	38 (54.3%)	33 (50.8%)	33 (50%)
Chemoembolization – non-hormone active tumors	23 (32.9%)	18 (27.7%)	18 (27.3%)
Chemoembolization – neuroendocrine tumors	10 (14.3%)	7 (10.8%)	12 (18.2%)
Radiofrequency ablation	5 (7.1%)	8 (12.3%)	3 (4.5%)
Uterine fibroid embolization	28 (40%)	30 (46.2%)	32 (48.5%)
Other tumor embolization	4 (5.7%)	2 (3.1%)	1 (1.5%)

The Spielberger State Anxiety questionnaire assesses anxiety and apprehension with 20 questions which are rated individually on a Likert-type scale from 0-4 and result in a summary score between 0 and 80.

All radiorequency ablations were for liver tumors with exception of one treatment for a pulmonary mass in the Empathy Group

Table 2

Descriptive statistics for ratings of anxiety and pain as a function of room time. Mann-Whitney rank sums tests of differences between groups.

Time (Min)	Standard			Empathy			Hypnosis			P values of Mann-Whitney Rank Sums		
	Median	IQR	N	Median	IQR	N	Median	IQR	N	S vs E	S vs H	E vs H
Ratings of anxiety												
0-15	**3.0**	0-6	*70*	**3.5**	2-6	*63*	**3.0**	0-5	*65*	0.550	0.331	0.131
15-30	**3.0**	0-5	*68*	**3.0**	1-5	*63*	**2.0**	0-4	*66*	0.985	0.016 *	0.019
30-45	**2.0**	0-4	*69*	**2.0**	0-4	*64*	**0.0**	0-3	*65*	0.825	0.015 *	0.006 *
45-60	**2.0**	0-4	*63*	**2.0**	0-3	*61*	**0.0**	0-2	*60*	0.466	0.036	0.125
60-75	**1.0**	0-4	*59*	**2.0**	0-3	*54*	**0.0**	0-3	*54*	0.873	0.103	0.129
75-90	**0.0**	0-3.5	*45*	**2.0**	0-4	*49*	**0.0**	0-2	*40*	0.265	0.276	0.012 *
90-105	**2.0**	0-4	*34*	**2.0**	0-4	*37*	**0.0**	0-2.6	*34*	0.697	0.142	0.050
105-120	**2.0**	0-3.5	*25*	**2.2**	0-4	*28*	**0.0**	0-3.5	*21*	0.675	0.424	0.272
120-135	**0.0**	0-3	*13*	**2.5**	1.1-4	*14*	**0.0**	0-3	*16*	0.140	0.750	0.107
135-150	**1.0**	0-5.5	*9*	**2.3**	0-3.5	*10*	**0.0**	0-1.5	*9*	0.834	0.145	0.055
Ratings of pain												
0-15	**1.0**	0-3	*70*	**0.0**	0-2	*65*	**0.0**	0-2.5	*65*	0.223	0.056	0.530
15-30	**1.0**	0-3	*68*	**1.0**	0-3	*65*	**0.0**	0-2	*66*	0.527	0.002 *	0.014 *
30-45	**2.0**	0-4	*69*	**1.0**	0-4	*64*	**0.0**	0-2	*66*	0.855	0.002 *	0.004 *
45-60	**2.0**	0-4	*63*	**2.0**	0-4	*62*	**0.0**	0-2.3	*61*	0.957	0.073	0.057
60-75	**2.5**	0-5	*58*	**2.0**	0-4.1	*54*	**0.0**	0-4	*55*	0.988	0.079	0.088
75-90	**3.0**	0-5.8	*45*	**3.5**	0-5.5	*49*	**1.5**	0-4	*41*	0.692	0.054	0.012 *
90-105	**3.0**	0-6.3	*34*	**4.0**	0-6	*37*	**2.0**	0-4	*34*	0.877	0.237	0.137
105-120	**2.0**	0-7.5	*25*	**3.0**	0.5-6	*29*	**1.0**	0-4	*21*	0.778	0.218	0.049
120-135	**3.0**	0-6.5	*13*	**5.0**	2.5-6.5	*14*	**1.0**	0-4	*17*	0.161	0.370	0.004 *
135-150	**3.0**	0-7	*9*	**5.0**	0.8-6.4	*10*	**0.0**	0-3	*9*	0.589	0.118	0.019

IQR – interquartile range (25^{th} to 75^{th} percentile), N – number of patients of whom data were obtained per interval

S – standard care, E – empathy H – hypnosis

Note: Because we did 3 tests on each variable, we accept p at 0.016. Tests that are significant at this level are denoted with an '*'.

Table 3

Adverse Events

	Standard (n=70)	Empathy (n=65)	Hypnosis (n=66)
Systolic blood pressure fluctuations >50 mm Hg with one value ≤105 mm Hg or de novo hypotension <80 mm Hg	**3**	**3**	**3**
Systolic blood pressure fluctuations >50 mm Hg with one value ≥180 mm Hg	**5** (1)	**12**	**3**
De novo diastolic hypertension >95 mm Hg	**0**	**2** (1)	**0**
De novo bradycardia	**1**	**4**	**1** (1)
Vaso-vagal reaction	**3**	**3**	**1**
Sustained tachycardia >100 beats/min	**1**	**2** (2)	**0**
Cardiac arrhythmia	**1**	**2**	**0**
Chest pain	**2**	**0**	**0**
Hypoxia with oxygen saturation <90%	**0**	**1** (1)	**0**
Shortness of breath	**0**	**2**	**0**
SUM	**18** (2)	**31** (7)	**8** (1)

Bold numbers indicate the main event that lead to inclusion of the patient in the adverse event category. Each patient was counted only once for the statistical analysis. When patients had more than one adverse event the additional events were indicated in plain type and parenthesis

Table 4

Delayed Complications (classification and numbering of the Society of Interventional Radiology Reporting Standards)

	Standard (n=70)	Empathy (n=65)	Hypnosis (n=66)
Minor Complications A. No therapy, no consequence (small hematomas)	**1**	**1**	**1**
Minor Complications B. Nominal therapy, no consequence	**1**	**1**	**2**
New right bundle branch block, telemetry overnight	1		
Transient Creatinine raise to 1.5 mg/dL			1
Pain control[+] (extended observation)			1
Rash		1	
Major Complications C. Require therapy, minor hospitalization[#] (<48 h),	**3**	**3**	**2**
Volume overload, shortness of breath			1
Extended nausea and vomiting[+] difficult to control	1	1	1
Pain difficult to control[+]	1	1	
Panic attack, SOB, tachycardia		1	
Chest pain	1		
Major Complications D. Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h)	**3**	**4**	**1**
Hypertensive crisis, encephalopathy			1
Hypertension, ECG changes		2	
Flank ecchymosis, hypertension, rigors		1[*]	
Ileus; prolonged inability to eat	2	1	
Confusion, encephalopathy	1		
Major Complications E. Have permanent adverse sequelae	**0**	**1**	**1**
Readmission for gastrointestinal bleed, syncope, and ascites 8 days later			1
Encephalopathy, renal failure		1	
Major Complications F. Death	1	1	0
Hepatorenal failure (POD 4)		1	
Exsanguination from ileostomy varices (POD 5)	1		

POD – post operative day, ECG – electrocardiogram, SOB – shortness of breath

[#]Since tumor interventions typically include one night postprocedure observation, time 0 for extended hospitalization started 24 hrs post procedure.

[+] Nausea, vomiting, pain, or temperature increases within the postembolizatation syndrome were not considered complications unless they were resistant to ordinary medical therapy and/or prolonged hospital stay.

[*] Patient died after discharge POD 28 from disseminated metastatic disease