Hypnosis and communication reduce pain and anxiety in peripheral intravenous cannulation Effect of Language and Confusion on Pain During Peripheral Intravenous Catheterization (KTHYPE), a multicentre randomised trial

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Hypnotic technique and communication reduce pain and anxiety in peripheral intravenous cannulation: KTHYPE, a multicentre randomised trial

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Key words: anaesthesia, anxiety, peripheral intravenous cannulation, hypnosis, pain, patient experience

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Editor's key points

Use of positive words can improve pain perception and subjective patient experience.

The KTHYPE trial is arandomised, parallel, single ~~simple~~-blind, multicentre study comparing the effects of three types of communication on pain, comfort and anxiety in preoperative patients during peripheral intravenous cannulation (PIVC).

Pain and anxiety were decreased and comfort perception increased after PIVC when positive communication and hypnosis were used.

This well-designed randomised controlled trial showed a significant benefit of hypnotic technique during a routine perioperative procedure.

ABSTRACT

Background: Clinicians traditionally warn patients of pain before peripheral intravenous cannulation (PIVC). However, using words related to pain or undesirable experiences can result in greater pain and anxiety. Use of positive words can improve pain perception and subjective patient experience. We aimed to compare the effects of three types of communication, including hypnotic communication, on pain, comfort and anxiety in patients during PIVC.

Methods: The KTHYPE trial is a randomised, parallel, single blind, multicentre study of patients undergoing PIVC on the dorsal face of the hand before surgery. Patients from three hospitals were randomly allocated to one of three groups: PIVC performed with hypnotic technique (hypnosis group), negative connotation (nocebo group) or neutral connotation (neutral group). The primary outcome measure was the occurrence of pain measured with a 0 to 10 numerical rating scale just after PIVC.

Results: Of the 272 subjects analysed (hypnosis n = 89; nocebo n = 92; neutral n = 91), pain after PIVC was lower in the hypnosis group (mean [SD], range) (1.5 [1.9], 0-5) compared with the neutral (3.5 [2.3], 0-9 ; $p < 0.0001$) and nocebo groups (3.8 [2.5], 0-10 ; $p < 0.0001$). While anxiety was higher and comfort lower before PIVC in the hypnosis group, anxiety decreased and comfort perception increased after PIVC when hypnosis was used.

Conclusion: This is one of the first well-designed randomised controlled trials showing a significant benefit of hypnotic technique during a routine procedure such as PIVC. The results could facilitate implementation of hypnosis in daily clinical care.

Trial registration: clinicaltrials.gov NCT02662322

Communication is decisive in creating a therapeutic alliance with the patient. Unfortunately, a routine procedure as frequent and simple as peripheral intravenous cannulation (PIVC) can be a source of stress and pain. Pharmacological interventions have been shown to reduce the pain associated with PIVC. A network metanalysis suggested that PIVC pain can be reduced by local anaesthesia [1]. However, local anaesthesia for cannulation is usually only offered to children, and fewer than half of clinicians follow this procedure for adults, [2 3] which is time-consuming[3] and has a high rate of puncture failure [2 4]. Psychological interventions have also been shown to reduce the pain and anxiety associated with PIVC in children [5 6 7]. Communication skills is recognized as a key element of care, [8] but unfortunately, clinicians often warn adult patients of pain using words with a negative connotation (i.e. “painful”, “sting”). This attitude is thought to be helpful and empathic. However, warning using language that refers to negative experiences is associated with a modification of pain and comfort perception[9 10]. Warning the patient that the act will be painful leads to more pain and anxiety and can create a nocebo effect [9-13] . On the contrary, use of positive words and sentences can benefit patient comfort [14 15]. Hypnotic communication uses positive suggestions and distractions to reduce the sensitive and affective dimensions of the pain experience. Hypnosis is a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion [16]. Indirect hypnosis or Ericksonian hypnosis is a method utilizing body language, conversation, metaphors and other hypnotic techniques to induce therapeutic behavioural change by indirect suggestion. It starts from the beginning of the relationship between therapist and patient. This therapeutic alliance is essential. The hypnotic confusion technique uses distraction to focus patients on an incongruous, unexpected element outside of their preoccupation of the moment. By distracting the conscious mind, the therapist is able to open the unconscious mind to hypnotic language and to take advantage of its induced suggestibility to deliver an indirect suggestion of comfort. A benefit of hypnosis has been shown for anxiety and pain[17-20], but only few methodologically rigorous studies applying minimally effective control conditions have been published[17 21]. We therefore assessed the

effects of hypnosis using positive words associated with a confusion technique on the subjective experience of PIVC when compared with a nocebo and neutral communication.

METHODS

Study design and Population

The KTHYPE study is a randomized, controlled, parallel-group, single blind, multicentre, international clinical trial conducted in three hospitals: Rennes University Hospital (Rennes, France), Saint-Gregoire Private Hospital (Saint Grégoire, France) and Cliniques universitaires Saint-Luc, Université Catholique de Louvain (Brussels, Belgium). The Rennes University Hospital Institutional Reviewed Board reviewed and approved this clinical investigation (N°ID-RCB 2015-A01353-46), which was registered at clinicaltrials.gov (NCT02662322). The study was approved by all local ethics committees (N°2015-A01353-46 — 2016 01 07).

Adult patients > 18 yr of age requiring a 20 G PIVC on the dorsal surface of the hand before a scheduled surgery were included. Non-inclusion criteria were: unable to communicate in French, history of difficult venous access, premedication, pregnant or breast-feeding women, legally protected (under judicial protection, guardianship or supervision, persons deprived of their liberty) and urgent surgery. In case of failure during the first attempt of PIVC, the patient would be excluded from the study. All eligible patients gave their written consent prior study participation.

Procedure

An information sheet about the study was given to all patients during the preoperative consultation. After arriving in the operating room, eligible patients were informed of the study by an anaesthesiologist not involved in the care of the patient and called an “anaesthesiologist researcher”. He/she was blind to the allocation group and proposed to the

patient to participate as follows: "*A peripheral intravenous cannulation is necessary for your anaesthesia. We currently investigate how different procedures are perceived during the venous cannulation process. If you accept to participate in this trial, we will ask you to evaluate your experience during venous cannulation.*"

Subjects were randomised in three groups (hypnosis, nocebo or neutral) using a computer-generated randomization table stratified by investigation site with a 1:1:1 ratio. Subjects were blind of the allocation group. The primary evaluation criterion was assessed by the patient him/herself (self-evaluation). The anaesthesiologist researcher assessed the presence of movements and/or vocalization during PIVC. During the study period, subjects and anaesthesiologist researchers were kept blind to the randomization group. The anaesthesiologist and the anaesthesiologist nurse both called clinicians in the study were different from the anaesthesiologist researcher and were not blinded. They did not participate in the assessment of subjects at any time.

In all groups, clinician's experience for PIVC was at least three years. No local anaesthesia was allowed before PIVC. Only one attempt was allowed and the clinician catheterizing was the only one talking to the patient at the time. In the hypnosis group, clinicians were anaesthesiologists or nurses with a diploma in therapeutic and hypnotic communication and a minimum of one year of experience. In the nocebo and neutral groups, clinicians were anaesthesiologists or nurses with no training in therapeutic communication and / or hypnosis. During the procedure, clinicians communicated with the patient in a structured and standardized way depending on the allocation group (Table 1). In the hypnosis group, clinicians applied classical non-verbal hypnotic tools adapted to the subject and indirect suggestion of comfort by body language. The whole procedure lasted < 5 min.

Outcomes

The primary outcome was occurrence of pain just after PIVC assessed using a numerical rating scale (NRS) [22]. Secondary outcomes were perception of comfort and anxiety before

and after PIVC measured with a validated NRS [23 24]. Pain, comfort and anxiety were self-evaluated by subjects minutes before and after PIVC. Subjects evaluated themselves before seeing any needle.

Data Collection

At each participating centre, data were collected and entered into the electronic web-based case report form (eCRF) by two investigators (NF, FR) blinded to the allocation group, under the supervision of the trial site investigators. Data collection was monitored by trained clinical research associates.

Data collected by the anaesthesiologist researcher were anthropometric (age, gender and body mass index), type of surgical procedures according to the classification of the American Heart Association (ACC/AHA)[25], standard of education and socio-economic category. In order to ensure blinded evaluation, the presence or not of spontaneous patient arm, face withdrawal, smile and/or an unprompted vocalization or comments were also recorded by the anaesthesiologist researcher.

Subjects were asked to quantify their pain, anxiety and comfort on 11-point NRS (0 = no pain – 10 worst imaginable pain experience, 0 = no anxiety – 10 = worst imaginable anxiety and 0 = no comfort – 10 = best imaginable comfort) just before (for anxiety and comfort only) and within 3 min after the completed peripheral intravenous cannulation.

Statistical analysis

Based on an expected mean (SD) NRS value of 4.4 (2.4) in the nocebo [13], We included 88 subjects in each group to show a decrease in NRS of 15% in the neutral group and 30% in the hypnosis group (effect size of 0.05), assuming an alpha risk of 5% and a power of 90% in a two-sided one-way analysis of variance (nQuery 8, V.8.3.1.0, Cork, Ireland). Based on the Dupta and colleagues who calculated sample size with a hypothesized 20% decrease in NRS [13], we considered that a 30% decrease in NRS would reflect a clinically relevant effect and that 15% would indicate a significant but less clinically relevant effect in the neutral

group as compared with nocebo. We included 10% more subjects to take into account expected cases of failure of the first attempt of PIVC, or 300 subjects to obtain a minimum of 264 included.

Statistical analysis was performed with SAS V9.4 (SAS Institute, Cary, NC, US). All data analyses were performed by researchers blinded to group allocation. Normal distribution was assessed by descriptive statistics and histograms. Quantitative variables are presented as mean (SD) for continuous variables and as number (%) for categorical variables. Analysis of study outcomes was performed by one-way analysis of variance for continuous variables and chi-square test or Fisher exact test for categorical variables. In cases of statistical significance, two-by-two comparisons were performed with a Bonferroni adjustment threshold for multiple testing. A sensitivity analysis taking into account the standard of education was also performed for the primary outcome using two-way analysis of variance in which the group:standard of education interaction was tested.

RESULTS

Between March 2016 and March 2017, a total of 294 patients were randomised (Figure 1) from Rennes hospital: 62 recruited / 50 analysed; St Gregoire Hospital: 132 recruited / 128 analysed and St Luc Hospital: 100 recruited / 94 analysed. First attempt cannulation failure was 6.5% leaving 272 subjects analysed (Hypnosis group n = 89; Neutral group n = 92; Nocebo group n = 91). Subject characteristics are presented Table 2. Study groups were similar in gender, body mass index, types of surgical procedures, standard of education or socio-economic category. Self-evaluation of pain, anxiety and comfort was performed within 3 min after the end of PIVC (2.5 [2.8] min) without differences between groups.

The primary outcome, pain after PIVC, was significantly lower in hypnosis group compared with the neutral and nocebo groups (Figure 2). This difference in pain after PIVC was still

significant after adjustment for standard of education. There was no significant difference in pain after PIVC between neutral and nocebo groups.

Subjects in the hypnosis group were less likely to spontaneously withdraw their arm or face (n = 1 (2%)) \ compared with the neutral group (n = 17 (31.5%)) or nocebo group (n = 15 (22.4%)) ($p < 0.05$ for both comparisons without difference between neutral and nocebo groups ($p = 0.78$)). Negative face (grimace in pain) was higher in the nocebo group (n = 32 (47.8%), $p < 0.01$) and neutral group (n = 27 (50%), $p < 0.01$) compared with the hypnosis group (n = 9 (18%)). Positive face (smile) was higher in the hypnosis group (n = 31 (62%) compared with the nocebo (n = 2 (3%), $p < 0.0001$) and neutral groups (n = 1 (2%), $p < 0.0001$). No difference between groups was observed for unprompted vocalization or comments.

Anxiety before PIVC was higher in the hypnosis group compared with the neutral group but not with the nocebo group (Table 3). Comfort before PIVC was lower in the hypnosis group compared with the neutral and nocebo groups. Anxiety after PIVC decreased in the hypnosis group but not in the nocebo and neutral groups. Comfort increased after PIVC in the hypnosis group and decreased in the neutral and nocebo groups. When anxiety and comfort after PIVC were adjusted to those before PIVC, anxiety after PIVC was significantly lower and comfort significantly higher in the hypnosis group compared with the neutral and nocebo groups (Figure 3). No differences were observed between neutral and nocebo groups.

DISCUSSION

To our knowledge, this is the first randomised controlled trial showing the benefit of hypnosis on a routine procedure as simple as PIVC. Pain and anxiety decreased and comfort perception increased after PIVC when hypnosis was used. Previous studies reported pain scores after 20 G PIVC placed on the dorsal surface of the hand similar to values observed in our control groups (neutral/nocebo)[26-28]. The levels of pain NRS obtained with hypnotic communication in our study were similar to those reported with local anaesthesia[26-28]. Therefore, hypnosis with confusion technique seems to offer a benefit

comparable to invasive pharmacological interventions. Moreover, this benefit was not associated with side effects and was not time-consuming (< 3 min). Our first attempt failure rate (6.5%) was lower than in previous studies (7-16%)[29 30]. The low rate of failure in our study could be explained by the lack of local anaesthesia, which can increase puncture failure, [28 30] and by the experience of the staff in our study. Our results also show that a hypnotic confusion technique could be applied without impacting the efficiency of PIVC. A previous study showed the influence of negative words on pain during blood sampling [31]. However, physicians involved in that study were not trained in hypnotic communication. The non-verbal part of the experience was then missing. In our study, only the verbal language could be standardized. Our therapists adapted complex non-verbal communication to each subject and indirect suggestions were induced from the outset with the therapeutic alliance.

Dutt-Gupta and colleagues [13] showed that warning patients of a 'sting' before PIVC may not be helpful. Comparing communication with positive or negative words, they reported no differences in pain and Likert scale scores. However, they reported (as a secondary outcome) less patients vocalizing pain during PIVC with positive communication. In our study, hypnotic communication produced decreased pain perception not only compared with the nocebo group but also with the neutral group. As the hypnotic process can play a crucial role in the modulation and perception of pain, our results show that use of positive words involving hypnotic communication could also reduce anxiety and improve comfort. Furthermore, pain perception, anxiety, and comfort were similar in the neutral and nocebo groups suggesting that a neutral attitude is as deleterious as a nocebo one. Our findings confirm that warning patients with nocebo and even neutral words, although made with good intent, induced discomfort. Hypnosis can be defined as an altered conscious state of focused attention that involves absorption, some dissociative elements, and an increased responsiveness to suggestion. In other words, the hypnotic cerebral process is well known to improve suggestibility. The verbal distraction and focalization included in the hypnotic confusion technique by saying something like "is your bike still going to the pool?" just before PIVC created confusion in patient's mind. The patient may ask "what did he/she say?" and at this time the patient is "dissociated" and focused on the meaning of the sentence rather than on the PIVC.

Overall patient satisfaction is correlated with communication and pain management [32] and can be improved with hypnosis[33] . In the perioperative setting, PIVC is one of the major sources of preoperative anxiety[34]. Comfort obtained by hypnotic communication before surgery may help improve patient satisfaction[17]. Hypnotic communication, or at least therapeutic communication, should be mandatory in the initial training of caregivers.

One limitation is that the study was single blinded. We chose to perform PIVC in the hypnotic group by non-blinded anaesthesiologists and nurses with a hypnotic communication diploma. We hypothesized that hypnotic communication would have too much influence on non-verbal communication to not impact the relation with patients. If clinicians with a hypnotic communication diploma are able to suggest comfort, they could also suggest pain and discomfort if they performed PIVC for neutral and nocebo groups. Another limitation is the restriction of the hypnotic group to anaesthesia providers with a hypnotic communication diploma. Whether the salutary effects of hypnosis are the same when providers not trained in hypnosis use the same technique needs further research.

Our study did not show the benefit of the hypnotic confusion technique *per se* as it was provided by clinicians with a hypnotic communication diploma. We cannot conclude that the hypnotic confusion technique provided by clinicians without a diploma would have any benefit. Indeed, Lang and colleagues [35] showed that hypnosis compared to attentive behaviour alone provides greater effects on pain and anxiety reduction during invasive medical procedures. Thius hypnotic communication involving a confusion technique may be more efficient than distraction alone to reduce pain and anxiety during PIVC. Further studies are necessary to test this hypothesis. Finally, anxiety was more important in the hypnosis group before PIVC compared with other groups. These differences happened despite randomization. However, subjects in the hypnosis group were less anxious and more comfortable after PIVC, which is what matters because it is what they will remember. When

patients are in a comfortable state, they are likely to stay in that state and uncontrollable anxiety is prevented[36]. In other words, a good experience with PIVC can determine the quality of the subsequent experience in the hospital.

In conclusion, the KTHYPE trial is the first randomised, multicentre study evaluating the effect of communication on pain, comfort and anxiety in surgical patients undergoing PIVC. It shows that hypnotic communication with a confusion technique compared to neutral or nocebo communication decreases pain and anxiety after PIVC. These results suggest that implementation of hypnosis into daily care and could lead to significant changes in the standard of care in anaesthesia.

Authors' c**ontributions**

NF, FB, FR, CW, HM, BL and HB contributed to the conception and design of the research protocol. NF was the principal investigator. He included patients in his centre and wrote the first draft of the manuscript. HB provided critical input in the writing of the manuscript. BL provided critical input for the methodology. NF, FB, FR, CW and HM included patients in their centres and critically revised and modified the manuscript. BL was responsible for the statistical analysis. All authors approved the final version of the manuscript.

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Declarations of interest

The authors have no relevant conflicts of interest.

Legends of the figures

Figure 1. KTHYPE study flow chart.

Figure 2. Self-evaluated pain after peripheral intravenous cannulation (PIVC) on an 11-point Numerical Rating Scale (NRS) (0 = no pain – 10 worst imaginable pain experience) for Hypnosis (n=89), Neutral (n=92) and Nocebo (n=91) groups. Median, first quartile and third

quartile are represented by box. Whisker plots represented 1.5 interquartile space associated with outliners for Hypnosis group. Mean is represented by rhomb. *** p<0.0001. NS = not significant.

Figure 3. Self-evaluated anxiety and comfort after peripheral intravenous cannulation (PIVC) on an 11-point Numerical Rating Scale (NRS) for Hypnosis (n=89), Neutral (n=92) and Nocebo groups (n=91). Median, first quartile and third quartile are represented by box. Mean is represented by rhomb. Whisker plots represented 1.5 interquartile range associated with outliners. *** p<0.0001. NS = not significant.

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Figure 1

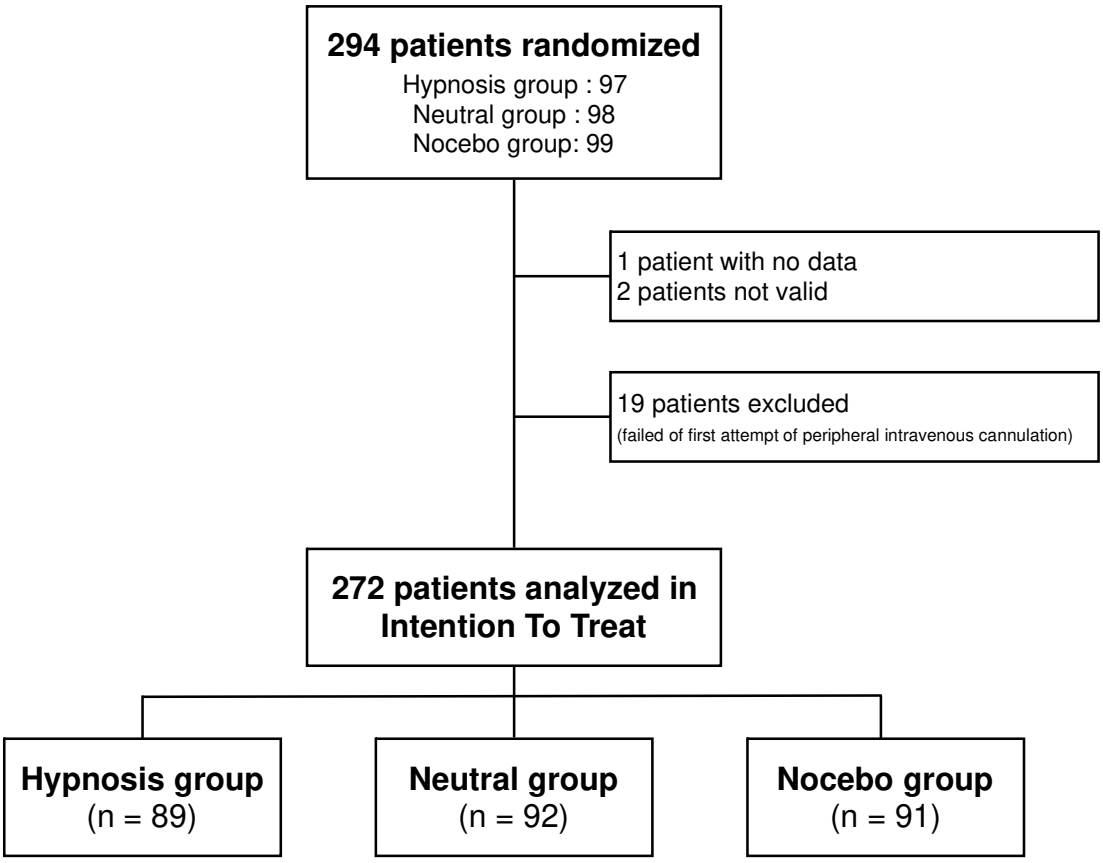
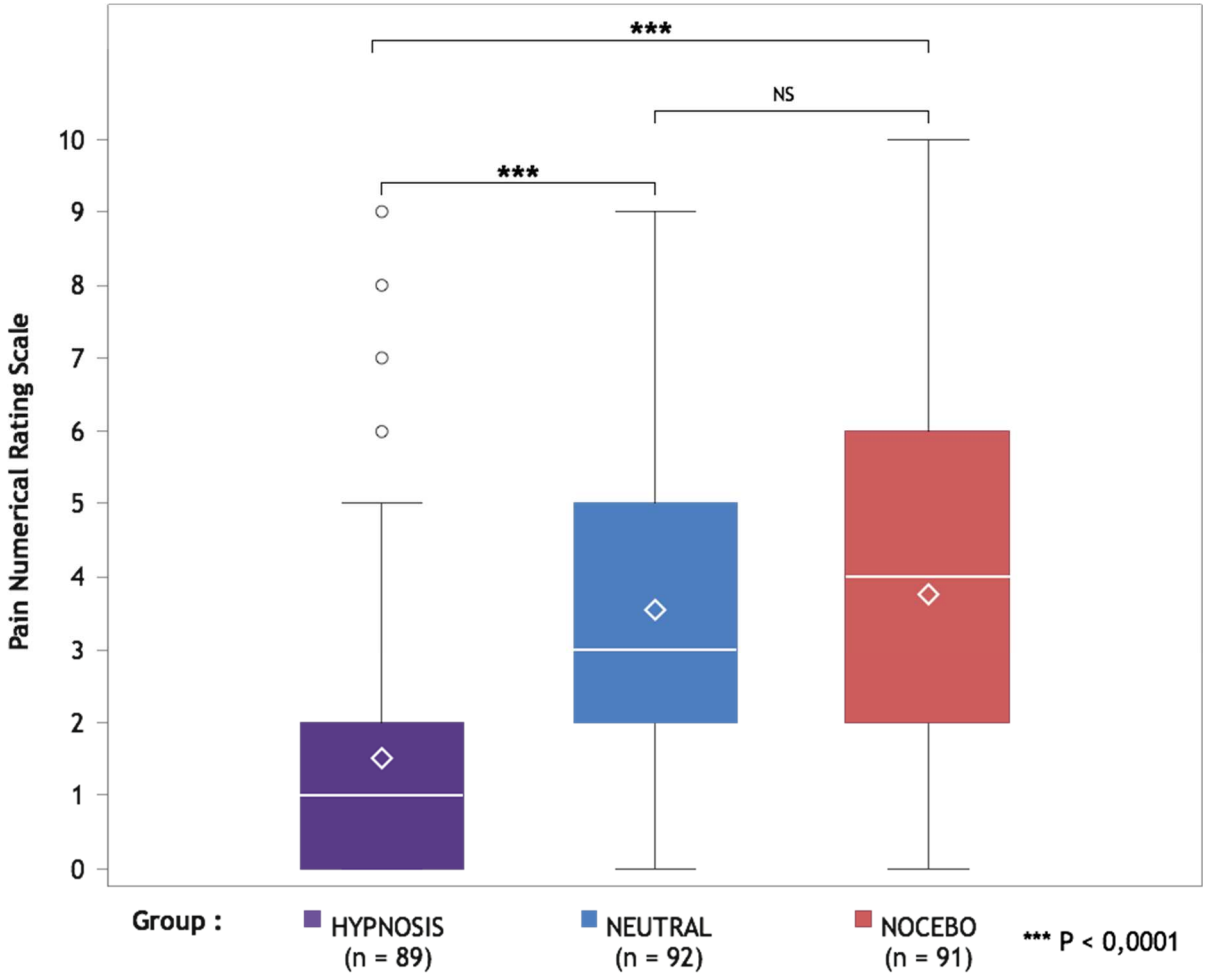

294 patients randomized
Hypnosis group : 97
Neutral group : 98
Nocebo group: 99
1 patient with no data
2 patients not valid
19 patients excluded
(failed of first attempt of peripheral intravenous cannulation)
272 patients analyzed in Intention To Treat
Hypnosis group
(n = 89)
Neutral group
(n = 92)
Nocebo group
(n = 91)

Figure 2


***
NS
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Pain Numerical Rating Scale
10
9
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Group :
HYPNOSIS
(n = 89)
NEUTRAL
(n = 92)
NOCEBO
(n = 91)
*** P < 0,0001

Figure 3

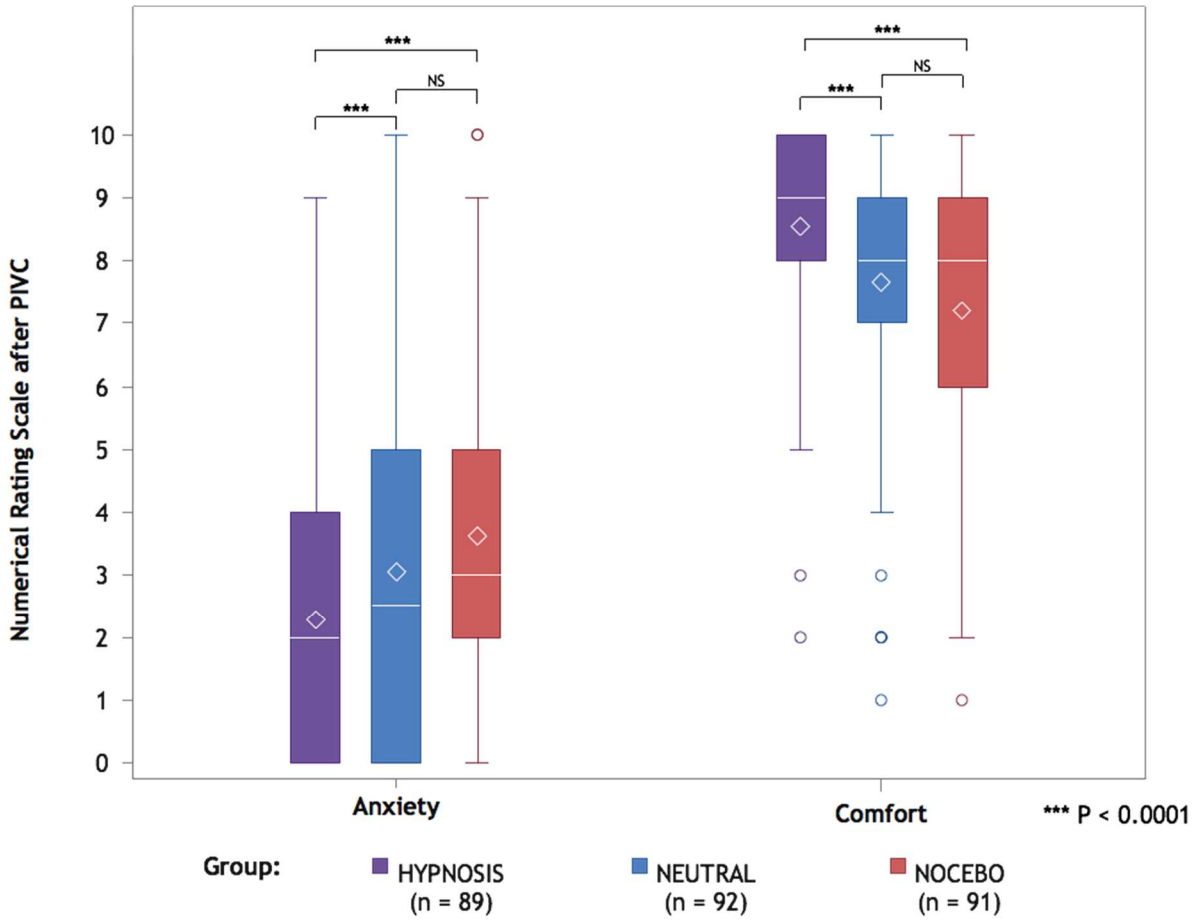
Numerical Rating Scale after PIVC
10
9
8
7
6
5
4
3
2
1
0
***
NS
***
***
NS
***
Anxiety
Comfort
*** P < 0.0001
Group:
HYPNOSIS
(n = 89)
NEUTRAL
(n = 92)
NOCEBO
(n = 91)

Table 1

Structured and standardized communication during peripheral intravenous cannulation.

	Placing tourniquet around the arm	**Decontaminating skin with light friction**	**Inserting peripheral intravenous catheter**
Hypnosis	“How did you come to the hospital?”	“How long did it take you to come here?”	“Is your bike still going to the pool?”
Neutral	“I am placing the tourniquet to dilate the vein.”	“I am decontaminating the skin.”	“I am putting the catheter in.”
Nocebo	“I am placing the tourniquet, it grips/squeezes hard!”	“It is cold!”	“Warning, I will sting. One, two, three, it stings!”

Table 2
Subject characteristics

	Total (n=272)	Hypnosis (n=89)	Neutral (n=92)	Nocebo (n=91)
Demographics				
Mean age (SD) - yr	54.5 (17.5)	56.2 ± 16.9	53.7 ± 16.9	53.7 ± 18.6
Sex (F/M) - %	55 / 45	54 / 46	52 / 48	60 / 40
Mean BMI (SD) – kg m^{-2}	25.7 (5.2)	26 ± 5.9	25.1 ± 4.3	25.9 ± 5.3
Surgery Procedure Risk (ACC/AHA) - no. (%)				
High	11 (4)	8 (9)	2 (2)	1 (1)
Intermediate	81 (30)	22 (25)	27 (29)	32 (35)
Low	180 (66)	59 (66)	63 (68)	58 (64)
Standard of education - no. (%)				
No qualification	26 (10)	10 (11.4)	11 (12.0)	5 (5.5)
School (US) / Secondary School (UK)	75 (28)	24 (27.3)	29 (31.5)	22 (24.2)
High school (US) / A-Levels (UK)	60 (22)	16 (18.2)	19 (20.7)	25 (27.5)
University (US) / Higher Education (UK)	110 (41)	38 (43.2)	33 (35.9)	39 (42.9)

There were no significant differences ($p<0.05$) between study groups. BMI, body mass index.

Table 3

Numeric Rating Scale (NRS) of anxiety and comfort self-evaluated before and after peripheral intravenous cannulation (PIVC) in Hypnosis group compared to Neutral and Nocebo groups.

	Hypnosis (n = 89)	Neutral (n = 92)	Nocebo (n = 91)
Before PIVC			
Anxiety	4.4 (2.6) [0-10] *	3.0 ± 2.6 (0-10)	3.5 ± 2.7 (0-10)
Comfort	7.5 ± 2.1 (2-10)*§	8.5 ± 1.6 (3-10)	8.3 ± 1.8 (3-10)
After PIVC			
Anxiety	2.3 ± 2.5 (0-9)*§	3.0 ± 2.9 (0-10)	3.6 ± 2.7 (0-10)
Comfort	8.5 ± 1.7 (2-10)*§	7.7 ± 2.2 (1-10)	7.2 ± 2.1 (1-10)
Pain	**1.5 ± 1.9 (0-9)***§	**3.5 ± 2.3 (0-9)**	**3.8 ± 2.5 (0-10)**
Difference before and after PIVC			
Anxiety	-2.1 ± 2.9£	+0.0 ± 2.3	+0.1 ± 2.3
Comfort	+1.0 ± 2.1£	-0.9 ± 1.9£	-1.1 ± 2.1£

NRS — mean (SD) [range]. Comparison of pain, anxiety and comfort NRS after PIVC are adjusted to those before. * p<0.05 *vs* neutral. § p<0.05 *vs* nocebo. £ p<0.05 before *vs* after