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Original Contribution

Visual/emotional stimuli and treatment with antidepressants alter Numerical Rating Scale score in patients with chronic pain☆,☆☆

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ABSTRACT

Study objective: To examine the impact of visual stimulation (exciting red and tranquilizing green) on the score of the Numerical Rating Scale (NRS) questionnaire in patients with chronic pain.
Design: Prospective randomized study.
Setting: Outpatient pain clinic of a university hospital.
Patients: Two hundred outpatients with chronic pain.
Interventions: Patients were randomly assigned to receive the NRS questionnaire printed on either red paper (red group) or green paper (green group).
Measurements: The questionnaire included 5 questions consisting of the NRS in the worst, in the least, and in the average pain during last week and the NRS at rest and on movement at present. Calculation of the sample size was based on power of 0.8 and $\alpha = .01$.
Main results: The NRS scores were not different between the 2 groups. In patients on antidepressants (n = 76) and with depression (n = 49), the NRS scores, except the NRS in the worst pain during last week score in patients on antidepressants, were significantly higher in the red group than in the green group (all $P \leq .040$). In the red group, the NRS scores were significantly higher in patients with than without depression (all $P \leq .003$), whereas there was no difference in the scores between patients of the green group with and without depression.
Conclusion: Our findings suggest that visual/emotional stimuli and treatment with antidepressants alter the NRS score in patients with chronic pain.

1. Introduction

The severity of chronic pain and efficacy of treatment are often evaluated using a 0-to-10 Numerical Rating Scale (NRS; 0 = no pain, 10 = worst pain possible) [1]. Although the pain intensity NRS has been validated as an outcome measure, little information is available on the factors that can modify the score of NRS. The NRS represents patient self-report, and the sole reliance on this scale sometimes hampers diagnosis and treatment.

Psychological changes such as hypnosis [2], expectation [3], attention [4], and emotion [5] are known to modulate the perception and processing of noxious stimuli. Furthermore, several investigators using functional neuroimaging techniques have reported that environmental pain-related visual and semantic cues or recalled pain experience can activate the pain matrix even when no painful stimulus is applied [6-8]. In fact, experiencing pain or merely anticipating it can induce anxiety [9]. The brain activity resulting from changes in pain intensity may reflect not only stimulus intensity but also emotional distress [10]. Especially, patients with chronic pain are overly sensitive to pain-related anxiety in addition to painful stimuli [11].

These evidences support our hypothesis that anticipatory emotional distress reinforces memorized pain, resulting in increased score on the NRS. We focused on the effect of color of the NRS questionnaire paper to test the hypothesis that visual/emotional stimuli can affect NRS assessment. For this purpose, we determined the impact of an exciting red questionnaire and a tranquilizing green questionnaire on the NRS

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score in patients with chronic pain [12]. In addition, we explored the effects of often used mood-modifying antidepressants and opioids on the NRS score.

2. Materials and methods

2.1. Subjects

The study patients were 200 consecutive outpatients who visited our hospital for relief of chronic pain. Patients were eligible for inclusion if they were 20 years or older, were capable of proper assessment of the severity of pain and condition, and had at least moderately troublesome pain of a minimum of 3 months' duration. Excluded from the study were patients with visual disturbances, such as visual loss, visual field defect, and color vision defect, to avoid the potential effects of such disturbances on the ability to read the questionnaire and distinguish differences in text colors. Also excluded were patients with encephalopathy, such as cognitive impairment, and those with learning disorders.

Written informed consent was obtained from each subject, and the study was approved by Kitasato University Hospital Ethics Committee and conducted according to the Declaration of Helsinki. This trial was registered with the University Hospital Medical Information Network (UMIN, #R000015483).

2.2. Study design

The concept of NRS and the study protocol were explained in details to the patient by a physician who was blinded to the details of patient background and patient group. Before randomization, patients were asked to provide the NRS score of the usual level of pain intensity without the questionnaire. Using a computer-generated block randomization code with stratification by sex, age, treatment with antidepressants and opioids, and initial (baseline) NRS score, patients were assigned at random to receive the NRS questionnaire printed on either red paper (red group) or green paper (green group). Text color (black), font type and size, and distribution of the characters were similar in the red and green questionnaires. The questionnaire included 5 questions consisting of the NRS in the worst, in the average, and in the least pain during last week and the NRS at rest and on movement at present.

Table 1
Patient characteristics

Patients' characteristics	Red group (n = 100)	Green group (n = 100)	Total (n = 200)
Female:male	51:49	54:46	105:95
Age (y)	63 (46-73)	64 (51-74)	63 (48-73)
Height (cm)	159 (152-167)	160 (153-168)	160 (152-167)
Body weight (kg)	59 (50-64)	56 (49-66)	58 (49-65)
Baseline NRS score	5 (4-6)	5 (4-6)	5 (4-6)
Patients with depression	28	21	49
Patients on oral medications			
Antidepressants	37	39	76
Opioids	51	53	104
Duration of pain (y)			
0.25-1	18	13	31
1-5	52	64	116
5-10	16	13	29
>10	14	10	24
Diagnosis			
Postherpetic neuralgia	17	15	32
Spinal canal stenosis	12	13	25
Complex regional pain syndrome	7	9	16
Others	64	63	127

Data are number of patients or median (25th and 75th percentile) values.
NRS = Numerical Rating Scale.

Table 2
Numerical Rating Scale; red vs green

	Red group (n = 100)	Green group (n = 100)	P
During the last week			
NRS-w	7 (5-8)	7 (5-8)	.391
NRS-a	5 (3-6)	4 (3-6)	.362
NRS-l	3 (2-4)	2 (1-4)	.064
At present			
NRS-r	4 (2-5)	3 (2-5)	.166
NRS-m	5 (3-6)	5 (2-7)	.199

Data are number of patients or median (25th and 75th percentile) values.
NRS, Numerical Rating Scale; NRS-a, NRS in the average pain during last week; NRS-l, NRS in the least pain during last week; NRS-m, NRS on movement; NRS-r, NRS at rest; NRS-w, NRS in the worst pain during last week.

2.3. Statistical analysis

We investigated the effects of antidepressants and opioids on the NRS score using the 2 colored questionnaires. In our hospital, approximately 50% of chronic pain patients usually take oral medications of antidepressants or opioids. A difference of at least 2 points of the NRS score was considered clinically significant [13]. Based on preliminary tests, we estimated the within-group standard deviation for NRS score of 2.5 points. Calculation of the sample size with a power of 0.8 and $\alpha = .01$ showed the need for 28 subjects (with antidepressants or opioids medications) and 56 control subjects for each color of the questionnaire. We considered a chance of about 10%-20% dropout and thus recruited 200 subjects in this study.

Continuous parameters were summarized as median (plus 25th and 75th percentiles), and categorical data were presented as numbers. Differences in the NRS score between the red and green groups and between treated and untreated patients were assessed by the Mann-Whitney U test. Furthermore, categorical variables were compared using the χ^2 test and Fisher exact test. Differences were evaluated with 2-sided tests, with an α level of .05. Analyses were performed with JMP Pro Ver. 10.0.2 statistical software (SAS Institute, Inc, Cary, NC).

3. Results

The study subjects included 105 men and 95 women. All patients completed the study and provided the required follow-up information. Table 1 shows the demographic and baseline clinical features of the patients. Forty-five (92%) patients of the 49 patients with depression were on antidepressants. Antidepressants were used for the treatment of neuropathic pain and/or depression. Patients of the 2 groups were similar in terms of age, sex, medications, and pain condition at baseline.

Tables 2-6 present the results of NRS. The NRS scores were not different between the red and green groups (Table 2). However, significant differences in the NRS score were noted in patients of the red group

Table 3
Numerical Rating Scale; red vs green on and off antidepressants

	Red group			Green group		
	Antidepressants		P	Antidepressants		P
	No (n = 63)	Yes (n = 37)		No (n = 61)	Yes (n = 39)	
During the last week						
NRS-w	7 (5-8)	7 (6-8)	.202	7 (4-8)	7 (4-8)	.740
NRS-a	4 (3-6)	6 (5-7)	.001	4 (2-6)	5 (3-6)	.814
NRS-l	2 (2-4)	5 (3-6)	<.001	2 (1-4)	2 (1-4)	.923
At present						
NRS-r	3 (2-5)	5 (4-7)	.001	3 (2-5)	4 (2-6)	.161
NRS-m	4 (3-7)	7 (5-8)	.001	4 (2-7)	5 (3-8)	.259

Data are number of subjects or median (25th and 75th percentile) values.
Abbreviations as in Table 2.