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RESEARCH REPORTS

CLINICAL AND EXPERIMENTAL EFFECTS OF INFORMATIONAL STRESS*

A. CRISTEA AND A. RESTIAN
Faculty of Pharmacy and Postgraduate Medical Training Center, Bucharest, Romania

SUMMARY

Under certain conditions, information may become stressful. In the initial stages of our research we found that informational stress can result in fatigue, anxiety, sleeplessness, and excitability. Later we found further symptoms, such as tachycardia, palpitations, chest pain, abdominal pain, increase or decrease of appetite, diarrhoea or constipation, muscle cramps, back pain, headache, tremor, dizziness, diaphoresis, tics, and so on. Some of these symptoms might be the result of cathecholamine increased secretion, others of a decrease of endogenous opioids. Because in the initial stage of stress analgesia may occur, we studied the clinical and experimental evolution of the pain threshold and its clinical manifestations. We found that after the initial analgesia, there follows a stage of hyperalgesia; the symptoms of this stage very much resemble those of the opioid abstinence syndrome. The evolution of this syndrome is enhanced by naloxone, an opioid antagonist, and it is attenuated by clonidine and propranolol, used in the treatment of opioid abstinence syndrome. Thus we demonstrated that in the latter stage of stress, there is diminished secretion of endogenous opioids and an acute tolerance to them.

KEY WORDS—Informational stress, endogenous opioids, endogenous opioid abstinence syndrome.

We have shown that under certain conditions, information may become a stressful factor.[1] By its quantity or quality, information may elicit some somatic disturbances.[2] In the initial stages of our research, we found that informational stress may result in fatigue, anxiety, sleeplessness and irritability.[3] Later, we found further symptoms caused by informational stress, such as tachycardia, palpitations, chest pain, abdominal pain, increase or decrease of appetite, diarrhoea, nausea, constipation, muscle pain, back pain, headache, tremor, dizziness, diaphoresis, tics, pallor or flushes and so on.[4] Some of these symptoms, such as anxiety, tachycardia, palpitations and high blood pressure, may be due to an increased secretion of catecholamines. Other symptoms such as headache, chest pain, abdominal pain, back pain and muscle pain may be due to an acute tolerance and a decreased secretion of endogenous opioids. However, in the first stage of stress there is a short period of analgesia due to an increased secretion of endogenous opioids.[5] We have therefore attempted to determine the secretion of endogenous opioids in informational stress by experimental and clinical trials.

MATERIALS AND METHODS

Clinical trial

For the clinical trial, we selected 24 healthy subjects of 20–25 years of age, who were exposed for one month to informational stress, during the summer examination session. The informational stress had both a quantitative and a qualitative aspect. The quantitative aspect consisted in the necessity of accumulating an important amount of information during the educational process. This information was estimated at about 2000 pages, which had to be learnt in a month. The qualitative aspect was represented by the emotions produced by the four examinations which followed. The subjects

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Address for correspondence: Dr Aurelia Cristea, Str Aviator Sanatescu, 43, Bucharest, 71324, Romania

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Table I—Kuhn and Friedel's test, completed by the authors for assessment of the exogenous opioid abstinence syndrome in animals

Symptoms	Score
1. Agitation	1
2. Sedation	1
3. Tachypnoea	1
4. Frequent micturation, diarrhoea	1
5. Erection of hair	1
6. Hyperexcitability	1
7. Tachycardia	1
8. Tremor	2
9. Hypersensitivity	2
10. Scratching	2
11. Vasodilatation	2
12. Eyelid ptosis	2
13. Chewing	2
14. Tooth grinding	3
15. Wet-dog shaking	3
16. Trunk stretching	3
17. Tail-tip gnawing	4
18. Vocalization	4
19. Curling up	4
Total	40

were under close scrutiny for clinical symptoms and pain threshold, as demonstrated by time of retraction of a finger from water heated to 58°C.

Experimental trials

For our experimental trials we used male albino rats. A group of 10 male albino rats were subjected for 60 minutes to informational stress by means of sound emitted by another group of 10 male albino rats that underwent elective electric shocks of 45, 60 or 90 volts, repeated with a frequency of approximately five shocks per minute.[6] The first group may be considered as the receiving group and the second as the emitting group. Analgesia was determined by time of retraction of the tail from water heated to 58.C. The behavioural changes were assessed by Kuhn and Friedel's test[7] for the study of opioid abstinence symptoms. This test was completed by us,[8] together with other symptoms frequently encountered, such as erection of hair, tail-tip gnawing, curling, and so on (Table 1).

Further experimental trials

In a further three receiving groups, each consisting of 10 albino rats, we administered, 45 minutes after the onset of the stress, naloxone, clonidine and propranolol. In the first group we administered naloxone, an antagonist of opioids, in a dose 0.5 mg/kg body weight. In the second group we administered clonidine in a dose 50 µg/kg body weight and in the third group propranolol in a dose 2 mg/kg body weight, as clonidine and propranolol are used in the treatment of opioid abstinence syndrome.[9,10]

RESULTS

Clinical

The follow-up of the 24 human subjects showed that the informational overexposure elicited the expected series of clinical disturbances as already enumerated. After a month of informational overexposure the number of symptoms increased from 62 to 217, that is, a 353 per cent increase (Table 2).

Regarding the evolution of the pain threshold,

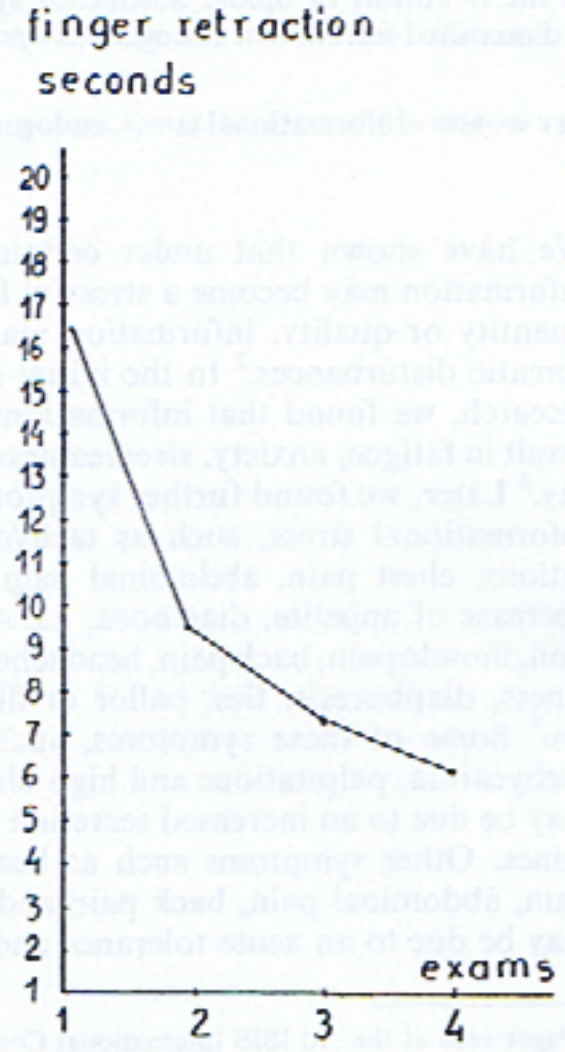

Fig. 1—Variation of endogenous analgesia as measured by the time of finger retraction of the 24 subjects determined after every exam

Table 2—Frequency and intensity of symptoms of 24 subjects exposed to informational stress (A, absent; L, light; M, medium; S, severe)

Symptoms	Intensity of symptoms							
	Before				After			
	A	L	M	S	A	L	M	S
1. Fatigue	20	2	2	—	8	8	6	2
2. Anxiety	21	2	1	—	10	8	4	2
3. Sleeplessness	22	1	1	—	15	5	3	1
4. Irritability	20	2	2	—	8	8	5	3
5. Palpitations	20	3	1	—	14	6	3	1
6. Tachycardia	19	4	1	—	8	10	5	1
7. Tachypnoea	23	1	—	—	21	1	2	—
8. Dispnoea	24	—	—	—	19	2	3	—
9. Nausea	23	1	—	—	19	2	3	—
10. Vomiting	24	—	—	—	22	1	1	—
11. Abdominal pain	22	1	1	—	16	3	5	—
12. Increased appetite	23	1	—	—	20	2	2	—
13. Decreased appetite	20	3	1	—	15	3	6	—
14. Diarrhoea	22	1	1	—	18	3	2	1
15. Constipation	21	1	2	—	19	3	2	—
16. Myalgias	24	—	—	—	17	4	2	1
17. Muscle cramps	21	2	1	—	18	2	3	1
18. Headache	16	6	2	—	8	6	6	4
19. Tremor	23	1	—	—	20	2	2	—
20. Dizziness	22	1	1	—	10	8	3	3
21. Flushes	20	1	3	—	15	3	5	1
22. Pallor	22	1	1	—	15	4	5	—
23. Chest pain	23	1	—	—	20	2	2	—
24. Perspiration	20	2	2	—	11	6	6	1
25. Tics	23	1	—	—	17	2	5	—
Total	538	39	23	—	383	104	91	22
Percentage	90	6	4	—	64	17	15	4

we noted that, in spite of large variations from case to case, the mean time of retraction of the finger after each exam dropped from 16.4 to 6.1, that is, a 62.8 per cent decrease (Fig. 1).

Experimental

Follow-up of the behaviour of the receiving group showed that it was significantly different during and after stress. During the informational stress, we observed initially a state of agitation, hair erection and tremor. After 15–30 minutes, the state of agitation was interrupted by periods of sedation, analgesia and vasodilatation. After the information had ceased, the characteristic symptoms of the opioid abstinence syndrome increased to 32.2 points. Towards the end of the postinformational stage, most of the rats were afflicted with depression and curled up.

Simultaneously with these specific symptoms, analgesia was replaced by a hyperalgesia, which reached a maximum of 63.3 per cent after 90 minutes.

Further experimental

In the naloxone-treated animals we noted an intensification of the symptoms to 39.5 points. At the same time the analgesia of the first stage was replaced by a hyperalgesia, which reached a 73.3 per cent peak, calculated by reference to the initial tail retraction time.

On the other hand, in the clonidine- and propranolol-treated animals, we observed an attenuation of symptoms. The test score was 7.8 points in the propranolol group and 8 points in the clonidine group (Fig. 2). The hyperalgesia of the postinformational stage at 90 minutes was 13.3 per cent in the propranolol group and 30 per cent in the clonidine group (Fig. 3).

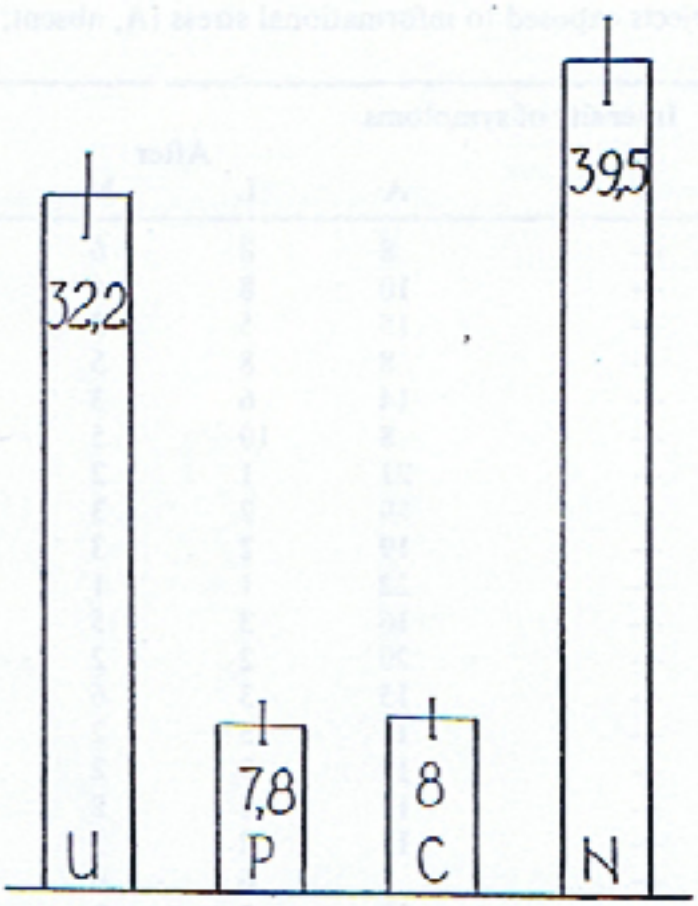

Fig. 2—The score of Kuhn and Friedel's test, completed by the authors, in untreated rats (U), in propranolol-treated rats (P), in clonidine-treated rats (C) and in naloxone-treated rats (N)

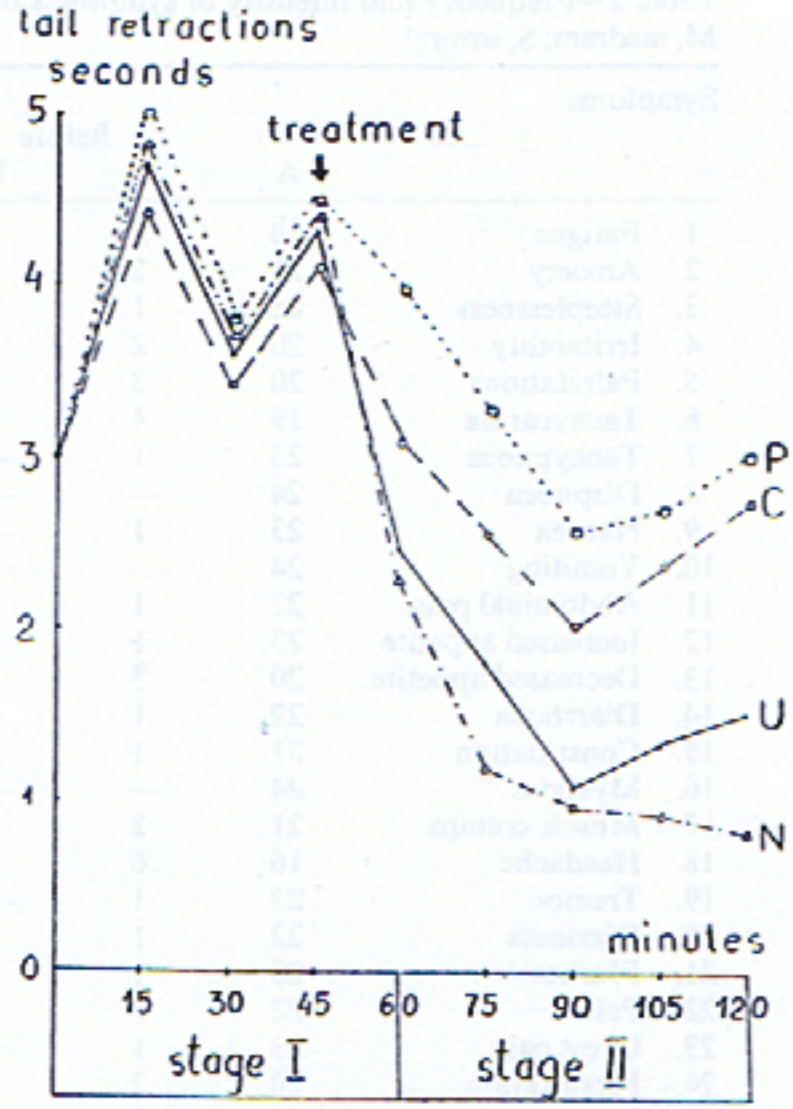

Fig. 3—The influence on hyperalgesia of propranolol treatment (P), clonidine treatment (C) and naloxone treatment (N) in comparison with the untreated rats (U)

Both in the clinical and experimental trials the differences were statistically significant.

DISCUSSION

Our results indicate that during a stress reaction there are clinical symptoms that are due either to increase or decrease of endogenous epioids. It has been shown by others that stress caused an increased secretion of endogenous opioids which induce analgesia.[11] But another function of these opioids is to the catecholamine and histamine systems.[12] By means of their sedative effects on heart rate and blood pressure, the endogenous opioids may balance the increase of heart rate and blood pressure due to catecholamines. However, the balance between the catecholamine and opioid systems is very unstable and the predominance of either of them may be dangerous for the organism. A catecholamine excess elicits tachycardia and high blood pressure, but an opioid excess may elicit respiratory depression and low blood pressure, as happens in shock, where naloxone administration is helpful.[13]

A low pain threshold and the emergence of symptoms like the opioid abstinence syndrome suggest that in the advanced stage of stress there is a decrease of endogenous opioids. Under these circumstances endogenous opioids can no longer balance the adrenergic system. The stress analgesia is replaced by hyperalgesia manifested by pain with different localizations. These symptoms could be prevented by clonidine and propranolol, as used in the treatment of the opioid abstinence syndrome.[9,10] The clinical manifestations of stress depend largely on the balance between the two systems. In any case, we consider that the advanced stage of stress is similar to an endogenous opioid abstinence syndrome. This is the outcome of both the decrease in secretion of endogenous opioids and an acute tolerance of endogenous opioids.[14]

All these findings correlate for a better explanation of stress issues and may offer new perspective for its treatment and prevention.

REFERENCES

1. Restian, A. Informational stress. *J. Roy Soc. Med.* 1990; **6**: 380–387.
2. Restian, A. *Patologia Informationala*. Edition Dacia, Cluj, 1977.
3. Restian, A. Le syndrome d'agression informationelle. *Agressologie* 1969; **2**: 85–93.
4. Restian, A. and Cristea, A. Manifestarile somatice ale solicitarilor informationale. *Rev. Med. Rom.* 1991; **6**: 305–310.
5. Willer, J. C., Dehen, H. and Cambier, J. Stress-induced analgesia in human. Endogenous opioids and naloxone reversible depression of pain reflexe. *Science* 1981; **212**: 689–695.
6. Cristea, A. Metodologia informationala in farmacologia experimentala. *Bul. Acad. Stiinte Med.* 1987; **1**: 37–38.
7. Kuhn, H. and Friedel, H. Uber der Nachweiss von Physical Dependenz bei Code in Behandelten. *Med. Exp.* 1967; **6**: 301–306.
8. Dobrescu, D., Cristea, A. and Belean, I. Cercetari privind ameliorarea sindromului de abstinenta la morfina. *Neurologia* 1978; **2**: 141–144.
9. Gold, M. S., Redmond, A. E. and Kleber, H. D. Clonidine blocks acute opiate-withdrawal symptoms. *Lancet* 1978; **2**: 599–602.
10. Kuryiama, K., Muramatsu, M. and Obkuma, S. Differential effects of morphine withdrawal on cerebral beta-1 and beta-2 adrenergic receptors. *J. Neurosci. Res.* 1981; **6**: 749–755.
11. Guillemin, R. and Redmond, D. E. Beta-endorphin and adrenocorticotropin are secreted concomitantly by pituitary gland. *Science* 1977; **235**: 1367–7.
12. Arbilla, S. Morphine and beta-endorphine inhibit release of noradrenaline from cerebral cortex. *Nature* 1977; **271**: 559–561.
13. Holaday, J. W. Cardiovascular effects of endogenous opiate system. *Am. Rev. Pharmacol.* 1983; **23**: 541–594.
14. Critea, A. and Popa Vaduva, G. Some possibilities to demonstrate and influence pharmacologically the interaction between the adrenergic and endogenous opioids system. Romanian Congress of Pharmacy, Bucharest 1989; 309–310.