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BRIEF REPORT

Pain threshold is reduced in depression

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Abstract

Pain and depression may share common neurochemical substrates, therefore the study of pain sensation in depression might be valuable in the investigation of the pathophysiology of depression itself. In order to investigate the sensation of pain in depression, we measured pain threshold and sensory threshold by means of a dental tester, comparing a group of depressed patients with healthy volunteers. The results showed the presence of a higher sensory threshold and pain threshold in patients than in controls. This may be related to a hyperfunction of the opiate system, which in turn might be primary or secondary to a decreased modulatory function of other neurotransmitters, in particular of serotonin, whose abnormalities in depressive states are well-documented.

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Introduction

Some data have shown an association between depression and idiopathic chronic pain which has been considered a sort of 'masked depression' (Magni and De Bertolini, 1983; Von Knorring et al., 1983) or, according to DSM-IV (1994), somatoform pain disorder. In particular, depressive symptoms seem to be quite common in idiopathic pain syndrome, although only 25% of the patients fulfil the criteria for major depressive disorder (Eberhard et al., 1989; Magni and De Bertolini, 1983). The clinical data are supported by a few reports on the presence of common biochemical alterations in depressed and chronic pain patients, such a shortened Rem latency (Blumer et al., 1982), a low cerebral spinal fluid concentration of 5 hydroxindoleacetic acid, the major serotonin (5-HT) metabolite (Almay et al., 1987), a low platelet monoamine- oxidase activity (Almay et al., 1987; Von Knorring, 1982, 1983), and a reduction of platelet [^{3}H]imipramine binding sites, which are associated with the 5-HT transporter (Eberhard et al., 1989; Magni et al., 1987; Mellerup et al., 1988). The last authors speculate that a low brain 5-HT turnover may underline and may lead to the development of both depression and pain.

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Furthermore, the analgesic properties of antidepressants, in particular of tricyclic antidepressants such as amitriptyline and imipramine (Eschalier et al., 1992, 1994; Max et al., 1987) and of selective serotonin reuptake inhibitors (SSRIs) (Eberhard et al., 1988) have been clearly demonstrated, especially in chronic pain, and they appeared not to be dependent upon their effect on mood (France et al., 1984).

Since both pain and depression may share common biological bases (Von Knorring et al., 1987, 1991), the study of pain sensation in depression might be valuable in the investigation of the pathophysiology of depression itself.

Because of its simplicity, noninvasiveness and acceptability, tooth pulp stimulation (a technique used in clinical dentistry for assessing pulp vitality) is a convenient test in experiments designed to investigate pain mechanisms (Ahlqvist et al., 1984, Chapman et al., 1976, 1977). The dental pulp represents an exclusively sensory system and a clear correlation between intradental nerve activity and pain perception, in response to graded stimulation applied to the teeth, has been reported (Ahlqvist et al., 1984). The pain threshold determined by this test is fairly reproducible within the same individual and can be altered by a variety of manipulations known to affect pain perception in the experimental animal, such as L-tryptofan supplementation, acupuncture, and transcutaneous stimulation (Seltzer et al., 1982). We report the results obtained in this test with a series of 13 depressed patients compared with healthy controls.

Subjects and methods

Subjects

Thirteen patients (4 male and 9 female; aged between 19 and 67 years; mean age 43.6 ± 15.8) with a clinical diagnosis of a major depressive episode, according to DSM-IV criteria (1994), consecutively admitted into the Day-Hospital of the Psychiatric Institute at Pisa University, were studied. Ten patients had been free of psychotropic drugs for one month and the remaining 3 were taking benzodiazepines (lorazepam, chlordesemetyldiazepam).

The control group consisted of 13 subjects (8 male and 5 female; aged between 27 and 33 years; mean age 30.7 ± 1.7) without any history of a major psychiatric disorder. The severity of depression was evaluated by means of the Hamilton Rating Scale for Depression (HRSD, Hamilton, 1960) and by a self-rating scale for depression ('Scala di Autovalutazione per la Depressione', SAD) standardized for the Italian population (Cassano and Castrogiovanni 1982). The total score on the HRSD was 18.3 ± 5.8 in patients and 0.4 ± 0.6 in controls. The total score on the SAD was 71.2 ± 15.6 in patients and 32.5 ± 4.7 in controls.

Methods

The procedure was described to all subjects as a test to assess pain sensitivity that could be of further clinical or scientific usefulness and all gave their informed consent to the study, which was approved by the Ethics Committee of Pisa University.

A commercial, noninvasive dental tester (American Analytic Technology, Missoula, MT, USA) was used. This instrument gives automatic intermittent bursts of electrical stimuli of negative polarity at increasing voltages, with a peak output voltage ranging from 15 to 300 V and a 2 MΩ load impedance. The intensity of the stimuli, expressed in arbitrary units (AU) on a relative scale between 0 and 80 was indicated on a digital reader in the instrument, not visible to the subject under examination. The performance of the instrument was checked every 4 months and remained stable throughout the study. All determinations were carried out in the morning between 9:00 and 10:00 hours, with the patient sitting on an odontologic chair and always by the same dentist (E.P.), who applied a probe to one of the superior incisive teeth under examination, blind to the clinical subject's conditions. The subjects were asked to indicate, by lifting a hand, when they started to feel pulp stimulation (as a prickling sensation) and when this became painful enough to require the interruption of stimulation; the corresponding values on display were taken as the sensory threshold and pain threshold. In several instances, the subjects did not report notable pain, even at the highest stimulus intensity of the instrument. For these subjects, in whom the pain threshold was not measurable since it was above the upper range of stimulation, the highest available value (80 AU) was given arbitrarily.

The difference between patients and controls was assessed by Student's t test (two-tailed, unpaired). The correlation between psychopathological rating scales and ST and PT was measured according to Pearson's analysis.

Results

Results are given as mean ± S.D. The sensory threshold (ST) was 52.3 ± 19.8 in patients and 34.6 ± 15.4 in controls, significantly higher in the first than in the second group ($t = 2.56$; $p = 0.02$). The pain threshold (PT) was 77.3 ± 6.9 in patients and 52.4 ± 20.1 in controls: also in this case, there was a statistically significant difference between the 2 groups, the pain threshold being higher in depressed patients than in controls ($t = 2.59$, $p = 0.02$).

No correlation between ST and PT and the psychopathological rating scales was observed.

Discussion and conclusions

The results of our research showed that a group of depressed patients revealed a higher sensory threshold and pain threshold than a group of healthy controls: these findings are suggestive of a reduced pain perception, as assessed by tooth pulp stimulation. Although the small number of patients did not permit reliable statistical analyses, no difference between drug-free patients and patients taking benzodiazepines was observed, as already reported (Boureau et al., 1991). Similarly, no age-effect on both sensory and pain threshold was detected in the patients.

Our findings replicated a previous research of our group (Marazziti et al., 1991) and a report of Adler and Gattaz (1993), but are in contrast with the reduction in pain threshold observed by others (Moroz et al., 1990; Ward et al., 1982).

Although it cannot be ruled out that perception of other sensations besides pain are reduced in depression, most evidence shows that, from a sensory point of view, the human tooth is an exclusively nociceptive system (Anderson et al., 1984; Byers et al., 1982) and that both pain and the so-called pre-pain elicited by electrical stimulation are mediated by the same type of afferents. The finding of a strong correlation between sensory threshold and pain threshold, observed in the pooled data, is also in keeping with a close functional relationship between the two measurements.

Pain is a function controlled by opiate peptides and possibly the changes in pain and sensory thresholds, observed in depressed patients, might be considered an index of dysfunction of the opiate system. Previously, increased plasmatic or cerebrospinal fluid levels of these peptides have been reported in depressed patients (Risch, 1982), however, opposite results have also been observed (Gerner and Sharp, 1982), so that opiate changes have been interpreted as a non-specific marker of stress rather than of depression. Similarly, any attempt to use opiate analogues or opiate antagonists, such as naloxone in depression, has been inconclusive (Angst et al., 1979; Gerner et al., 1980; Hollister et al., 1981).

Alternatively, a lower pain perception in depression might be attributable to dysfunctions of other systems, in particular, of the serotonin system, which plays a role in modulating pain (Basbaum and Fields, 1978; Roberts, 1984) and appears to be involved in the pathophysiology of depression (Gerner and Sharp, 1982; Seltzer et al., 1982; Van Praag, 1978). A decreased function of the serotonin system might lead to a relative increase in the function of other systems which are under its control, such as that of opiates.

Future studies should investigate the possible correlation between serotonergic markers and pain threshold in depression.

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