Evidence for Involvement of Central Noradrenergic Activity in Crying Proneness

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Crying as a response to emotionally-charged situations varies greatly among individuals, genders, and cultures. Information on the neural systems involved in crying behavior comes mainly from studies of pathological laughing and crying in patients after brain injury. The authors assessed crying proneness (CPR) as expressed by the score on the "crying easily" item of the SCL-90 questionnaire in 65 men and 105 women subjects in whom lumbar puncture was performed for diagnostic reasons. None of the subjects showed pathological laughing or crying. The authors estimated the levels of the main metabolites of noradrenaline (MHPG), serotonin (5-HIAA), and dopamine (HVA) in CSF, and searched for associations to CPR score. Subjects with high CPR showed significantly lower MHPG levels than subjects with low CPR, and no differences in 5-HIAA or HVA levels. Higher frequencies of women were found in the subgroups with high CPR. The "crying easily" score was positively associated with the Interpersonal Sensitivity subscale of the SCL-90 questionnaire in female but not in male subjects, indicating the cultural dimension of crying behavior, while it was not associated with the Depression subscale score. It is suggested that central noradrenergic mechanisms control the threshold for tear production in normal crying behavior.

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Crying is considered to be a unique human expression, usually as a response to emotionally-charged situations with negative but also with positive contexts,[1] as well as a response to physical pain. There is considerable variability among individuals in the frequency and intensity of "normal" crying; that is, in crying proneness (CPR), which includes the degree of control people have over their tears. It is negatively associated with emotional stability[2] and seems to appear as a familial tendency toward excessive emotionality.[3] In addition to the fact that crying frequency is higher in women than in men,[2] there are considerable differences among cultures in CPR and how one feels after a crying episode,[4] the differences being related to the Masculinity–Femininity cultural dimension of Hofstede[5] that refers to the distribution of roles between the genders.

Although increased crying frequency is related to depressed mood, the relationship of excessive crying to

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depression seems to lack a robust empirical foundation.[6] This, in addition to the fact that women report a higher crying frequency and crying proneness than men,[2] has led to the suggestion that crying should be removed from the diagnostic criteria for depression.[7] Crying is included as a separate item in the evaluation of depression in Beck Depression Inventory,[8] where changes in relation to previous crying behavior of the patient are considered for the evaluation, but the highest score is given when the patient cannot cry at all. Thus, the score on crying correlates poorly with the total depression score.[9] A "crying easily" item is included in the depression subscale of the SCL-90,[10] whereas crying behavior in the Hamilton Rating Scale for Depression[11] is considered in the evaluation of the Depressed Mood item, together with Feeling of Sadness. However, the author mentions that the tendency to weep must always be considered against the cultural background, and patients may also "go beyond weeping."

In addition to "normal" crying of healthy individuals, excessive crying has long been observed in certain neurologic disorders, sometimes together with excessive laughing. This "pathological" crying is characterized as episodes of uncontrollable emotional expression that occur without specific stimuli and are not consonant with a matching mood state, or even occur in contrast to it.[3] Such episodes have been documented in patients with amyotrophic lateral sclerosis, multiple sclerosis, in degenerative diseases, and after stroke or after traumatic brain injury.[1,12] The nature and the underlying physiological mechanisms of pathological crying have not been elucidated, resulting in a controversy about the terminology used by several authors to describe a higher-than-expected crying frequency and intensity. The terms "pathological laughing and crying," "pseudobulbar affect," "involuntary crying or laughing," "involuntary emotional expression disorder," "emotional dyscontrol," "emotional lability," "pathologic expression of affect," and others, are used in the literature. Nieuwenhuis-Mark et al.[1] propose the use of the term "excessive crying" to describe the phenomenon for the time being, since they consider it premature and unnecessary to characterize it as "pathologic" or as a "disorder." Parvizi et al.,[13] on the other hand, prefer to use the term "pathological laughing and crying (PLC)," since it has been favored historically in the literature, and this term will be used in the present study.

There is limited information on the involvement of neurotransmitter systems in crying behavior. Although it is considered as a parasympathetic activation,[14] the behavior is controlled by higher centers, and several limbic, frontal, brainstem, and other brain regions have been implicated in excessive crying.[1] Most for the information available is based on studies of PLC in neurologic patients, indicating involvement of serotonin, dopamine, and glutamate, as well as norepinephrine and acetylcholine. The precise roles of these neurotransmitters, however, remain undefined.[15] Drugs used for the treatment of PLC in neurologic patients[16] include tricyclic antidepressants (imipramine, amitriptyline, nortriptyline), serotonin reuptake inhibitors (SSRI), and serotonin-noradrenaline reuptake inhibitors (SNRI), indicating involvement of monoaminergic neurotransmitter systems, although the opinion has been expressed that the effectiveness of tricyclic antidepressants may be due to their anticholinergic properties.[17] One study reported reduced concentration of homovanillic acid (HVA), the main dopamine metabolite, and normal 5-hydroxyindoleacetic acid (5-HIAA), the main serotonin metabolite, in cerebrospinal fluid (CSF) of stroke patients with PLC, which led to the therapeutic use of *L*-dopa,[18] but these findings have not been replicated since. In patients with PLC after stroke, lower-than-control binding capacities of 5-HT(1A) serotonin receptor were reported,[19] as well as lower serotonin transporter densities.[20] Investigating which neurotransmitters (other than serotonin) are involved in PLC is one of the suggestions for future research proposed by the American Neuropsychiatric Association Committee on Research.[13]

Information on the modification of crying behavior in healthy subjects is sparse. Scoppetta et al.[21] reported improvement in tearfulness and uncontrollable fits of weeping in two healthy subjects and three subjects with moderate depression. All five gained control over their emotions after only a few days of treatment with SSRIs, too short a time to be related to the antidepressant effects of the drugs. A reduction in crying frequency and severity within 2 to 3 days after treatment with SSRIs has been also reported in neurological patients with "emotional incontinence."[22]

In this study, we searched for possible associations of crying proneness to central noradrenaline, serotonin, and dopamine turnover in subjects in whom lumbar puncture was performed for diagnostic reasons, and CSF was available for the estimation of

neurotransmitter metabolite levels. The SCL-90 questionnaire was administered, and the response to the item "crying easily" was taken as a measure of crying proneness.

SUBJECTS AND METHODS

We included in the study 170 subjects (65 men and 105 women) in whom lumbar puncture was performed for diagnostic reasons in the Neurologic Clinic of the Athens University Medical School, Eginition Hospital, and CSF was available for the estimation of neurotransmitter metabolites. Informed consent was obtained from all subjects, and the protocol of the study was approved by the Ethics Committee of the Hospital. Because of possible influences of drugs on neurotransmitter turnover, we only included subjects who were not taking any drugs at the time of assessment (145 subjects), or were either on thyroid replacement therapy (16 subjects), being euthyroid, or on minor tranquilizers (9 subjects). The study sample consisted of 1) 24 subjects (16 men) who were evaluated for possible neurosyphilis and were found negative, being asymptomatic, with positive treponemal tests in the serum but negative CSF findings and normal MMSE; 2) 16 subjects (7 men) who were found negative in their evaluation for possible multiple sclerosis (MS), having a few nonspecific T2 lesions on MRI and normal neurological examination, CSF analysis, and visual evoked potentials; 3) 51 subjects (16 men) who were diagnosed as having Clinically Isolated Syndrome (CIS) suggesting of MS; and 4) 79 patients (26 men) with relapsing–remitting or progressive MS. Diagnoses were made according to Polman et al.[23] for MS and according to Miller et al.[24] for CIS. Subjects ranged in age from 18 to 64 years, with mean age 37.8 (standard deviation [SD]: 10.2) years; 39.4 [10.1] for men and 36.8 [10.2] for women).

Lumbar puncture was performed in the lateral recumbent position between L3 and L4 or L4 and L5 after an overnight fast. The CSF fraction from 3rd to 5th ml was used for estimation of the metabolites, centrifuged to remove cells, and kept at –30°C until analysis, done within 3 months from sampling.

The levels of the neurotransmitter metabolites were estimated by high-pressure liquid chromatography (high-performance liquid chromatography) with electrochemical detection, all three in the same run.[25] A 4.6 x 250 mm column was used (Waters Spherisorb ODS2), and the mobile phase consisted of acetate buffer pH 5.2 with 10% methanol. For each sample, an aliquot of CSF was directly injected into the high-performance liquid chromatography system, and subsequently a second aliquot with added standards corresponding to 5 ng/ml for MHPG, 10 ng/ml for 5-HIAA, and 20 ng/ml for HVA in the CSF sample. The concentrations of the metabolites were calculated from the differences in peak heights between the sample with, and the sample without standards.

For the evaluation of the data, we compared the CSF metabolite levels among subgroups built according to the score (0, 1, 2, 3, or 4) on the "crying easily" item of the SCL-90 questionnaire, using analysis of variance (ANCOVA), with age as covariate. We also searched for relationships between CPR and the scores on the nine subscales of the questionnaire by performing multiple-regression analysis, with the dependent variable the score on the "crying easily" item, and independent variables the mean score in the nine subscales of the SCL-90 questionnaire. For the subscale Depression, we calculated the mean score, excluding the "crying easily" item. Ridge regression was used to control for intercorrelations between independent variables.

RESULTS

The CSF levels of the three metabolites in subgroups of subjects according to their score in the "crying easily" item are shown in Table 1. No differences in the serotonin (5-HIAA) and dopamine (HVA) metabolites were found, whereas the noradrenaline metabolite (MHPG) was reduced in the subgroups with a score ≥ 2, as compared with the subgroup with a score of 0. The frequencies of male and female subjects in the subgroups are also shown in Table 1, with women showing higher frequencies in the subgroups with high scores. The difference in the distributions between men and women was highly significant (Yates' chi-square=21.81; df=4; p=0.0002).

The number of male subjects with "crying easily" scores >2 in our sample was low. Of the 65 male subjects studied, only 4 had a score of 3, and only 1 had a score of 4 (Table 1). In order to examine whether the association of low CSF MHPG to high CPR is valid for both sexes, and since there were no differences in the metabolite levels between men and women in the subgroups with scores of 0 or 1, we merged the data,

TABLE 1. Number of Subjects and CSF Neurotransmitter Metabolite Levels (ng/ml) in Groups According to the Score on the "Crying Easily" Item of the SCL-90 Questionnaire

	Men		Women		M + W			
Score	N	%	N	%	N	MHPG	5-HIAA	HVA
0	37	57	27	26	64	7.16 (2.16)	17.7 (8.8)	27.8 (11.9)
1	17	26	22	21	39	6.71 (1.85)	16.1 (7.1)	28.8 (14.4)
2	6	9	19	18	25	6.12 (1.89)*	17.7 (7.2)	25.4 (9.3)
3	4	6	23	22	27	6.13 (1.77)*	15.7 (6.0)	28.36 (10.5)
4	1	2	14	13	15	5.81 (0.90)*	16.4 (5.5)	28.7 (5.5)
					$F_{4, 165}$	2.81	0.54	0.37
					p	0.027	NS	NS

Values are mean (standard deviation), unless otherwise indicated. The calculated percentages highlight the differences in frequencies between genders. MHPG: main metabolite of noradrenaline; 5-HIAA: main metabolite of serotonin; HVA: main metabolite of dopamine.
*> Significantly lower (planned comparisons, $p < 0.025$) than the group with score of 0.

TABLE 2. CSF Levels (ng/ml, mean [standard deviation]) of the Metabolites of Noradrenaline (MHPG), Serotonin (5-HIAA), and Dopamine (HVA), According to the Score on the "Crying Easily" Item of the SCL-90 Questionnaire

Score	N	%	MHPG	5-HIAA	HVA
All subjects					
Low	103	61	6.98 (2.05) (2.60-12.5)	17.1 (8.2) (4.60-46.4)	28.2 (12.9) (9.4-65.0)
High	67	39	6.06 (1.65) (3.13-10.8)	16.6 (6.3) (5.40-31.3)	27.3 (9.2) (10.6-53.7)
$F_{1, 168}$	9.67	0.15	0.23		
p	0.002	NS	NS		
Men					
Low	54	83	6.98 (2.17) (3.13-12.5)	16.6 (8.9) (4.6-46.4)	27.2 (12.6) (9.4-65.0)
High	11	17	5.33 (1.22) (3.13-8.14)	14.3 (7.8) (5.4-31.3)	24.0 (10.1) (12.2-38.3)
$F_{1, 63}$	5.81	0.62	0.65		
p	0.018	NS	NS		
Women					
Low	49	47	6.99 (1.93) (2.6-12.2)	17.6 (7.3) (4.9-35.0)	29.2 (13.2) (10.0-64.0)
High	56	53	6.20 (1.69) (3.33-10.8)	17.1 (6.0) (6.4-30.2)	28.0 (8.9) (10.6-53.7)
$F_{1, 103}$	5.02	0.17	0.32		
p	0.027	NS	NS		

Subjects were merged in two groups, with Low (0 or 1) or High (2, 3, or 4) score. Evaluation of the differences was by analysis of variance. Frequencies of men and women in the two groups are significantly different (Yates' chi-square=20.79; $p < 0.0001$). Minimum and maximum levels of the metabolites in each group are given in parentheses.

building two groups, one with low (score 0 or 1) and the other with high scores (2, 3, or 4), and compared the metabolite levels between these two groups for the whole sample and separately for male and female subjects. No differences were found either for 5-HIAA or for HVA levels, whereas MHPG levels were lower in the groups with high CPR scores for the whole sample ($p=0.002$), as well as for men ($p=0.018$) and women ($p=0.027$) when analyzed separately (Table 2).

In order to search for associations of crying proneness with SCL-90 subscales score, we performed multiple-regression analysis, with the dependent variable the score on the "crying easily" SCL-90 item, and independent variables the mean scores in the nine subscales of the questionnaire; that is, Somatization, Phobic Anxiety, Obsessive-Compulsive, Hostility, Anxiety, Paranoid Ideation, Interpersonal Sensitivity, Psychoticism, and Depression. The mean score for each subscale is calculated as the sum of the scores on the items included in the subscale, divided by the number of the subscale items, which varies for the nine subscales, from 6 to 13. For the subscale Depression, since the score on one of its items (crying easily) is used as the dependent variable of the analysis, we calculated the sum of 12 items from the 13 that comprise the subscale, omitting the score on the "crying easily" item, and divided by 12, to build the mean score. Performing multiple-regression analysis for the total sample of 170 subjects, a highly significant multiple correlation was found ($R=0.5367$; $F=7.19$; $p=0.001$; Table 3). Significant association with CPR was found only on the subscale Interpersonal Sensitivity. When the analysis was performed separately for men and women, the association was significant only for women. The association of "crying easily" with the Depression subscale score was not significant in any group.

DISCUSSION

The reported "crying easily" score of the SCL-90 questionnaire (possible answers: Not at All, A Little Bit, Moderately, Quite a Bit, and Extremely, with scores 0 to 4 points) expresses the proneness of the individual to cry during the past weeks, a period close to the time of the lumbar puncture. This self-reported crying prone-

TABLE 3. Multiple-Regression Analysis With Dependent Variable the Score on the "Crying Easily" Item of the SCL-90 Questionnaire and Independent Variables the Score on the Nine Subscales

	All		Men		Women	
N	170		65		105	
R	0.5367		0.4409		0.5901	
sF [df]	7.19 [9, 160]		1.47 [9, 55]		5.64 [9, 95]	
p	0.0000		0.18		0.0000	
	β	p	β	P	β	p
Somatization	0.095	NS	0.008	NS	–0.005	NS
Depression	0.177	0.12	0.285	NS	0.125	NS
Phobic Anxiety	–0.025	NS	0.072	NS	–0.097	NS
Obsessive-Compulsive	0.134	NS	–0.045	NS	0.217	0.10
Hostility	0.003	NS	NS	NS	0.009	NS
Anxiety	–0.025	NS	–0.007	NS	–0.068	NS
Paranoid Ideation	0.119	NS	0.020	NS	0.224	0.09
Interpersonal Sensitivity	0.244	0.015	–0.066	NS	0.301	0.015
Psychoticism	–0.164	.07	0.039	NS	–0.173	0.14

ness includes the dimension having control over tear-shedding; that is, the cultural component of the behavior, which is manifested in the differences of frequencies in low or high scores between men and women. It should be noted that the item "I find myself crying very easily" is included in the self-report measure of affective lability proposed by Moore et al.[26] in their Labile Tearfulness Subscale, which consists of three items, and is the item with the higher factor-loading. Although the relationship of CPR to PLC in neurological patients remains to be examined, CPR does not represent involuntary emotional expression, since the propensity to cry in emotionally-charged states is considered to be a personality trait and not a symptom of underlying disease. In clinical assessment, none of our study subjects showed pathological laughing or crying, although we included patients with MS. According to Feinstein et al.,[27] 10% of patients with definite MS are expected to manifest PLC. The authors notice that the number of MS patients with PLC increases as the disease progresses, and occurs around 10 years after the diagnosis of the disease. In our sample, there were 79 patients (26 men) with definite MS, none of them showing PLC. This could be explained by the fact that in only 12 (15%) of them was the disease duration over 10 years, and that we studied only patients who were drug-free, excluding those under treatment with psychoactive drugs.

The question of a possible association between CPR and PLC, that is, the idea that neurological patients who develop PLC after disease onset do have a higher CPR as a personality characteristic, has not been addressed up to now. Parvizi et al.,[13] speaking of a dysregulation of emotional expression in both normal and pathological crying, note that the actual behavior of PLC is often indistinguishable from normal acts of laughter and crying. It can be expected that patients who develop PLC after brain injury may have high CPR as a personality trait, but this remains to be shown in future research.

The relationship of CPR to the subscales of SCL-90 gave interesting results. It is not associated with the depression score, confirming previous results that CPR is a personality trait, rather than being related to mood or affect. The only significant association was to the Interpersonal Sensitivity (IS) subscale in women but not in men, a finding that supports the notion that CPR is culturally defined. This (IS) subscale is described as a dimension that focuses on feelings of personal inadequacy and inferiority in comparison with others, including uneasiness and discomfort during interpersonal interactions. In Hofstede's[28] cultural dimension of Masculinity–Femininity, in masculine societies, women are supposed to be tender, take care of relationships, and deal with feelings. Girls cry; boys don't. Hofstede has evaluated the relative strength of this dimension for 50 countries, on a scale from 0 to 100. For Greece, a moderate Masculinity Index of 57 was found, the index ranging from 95 for Japan to 5 for Sweden.

The finding of reduced central noradrenergic activity in subjects with high crying proneness, refers to normal crying behavior as a response to emotionally-charged situations that occur in subjects who do not show any involuntary impulsive behavior, as is the case for patients with PLC. Impulsiveness has been related to reduced serotonergic function,[29] and we did not find any relation of serotonin turnover to CRP in our sample. Possible impaired noradrenergic function in PLC remains to be examined in future studies. Indications

of noradrenergic involvement in PLC are provided in short reports where the SNRI drugs venlafaxine,[30] mirtazapine,[31] or duloxetine[32] were used successfully in patients with PLC who failed to respond to SSRIs. In these cases, the amelioration of symptoms could have been achieved by an increase in the threshold for tear production by increasing noradrenergic activity.

References

1. Nieuwenhuis-Mark RE, van Hoek A, Vingerhoets A: Understanding excessive crying in neurologic disorders: nature, pathophysiology, assessment, consequences, and treatment. Cog Behav Neurol 2008; 21:111–123
2. Peter M, Vingerhoets AJJM, Van Heck GL: Personality, gender, and crying. Eur J Personality 2001; 15:19–28
3. Cummings JL: Involuntary emotional expression disorder: definition, diagnosis, and measurement scales. CNS Spectrums 2007; 12(suppl 5):11–16
4. Becht MC, Vingerhoets AJJM: Crying and mood change: a cross-cultural study. Cogn Emot 2002; 16:87–101
5. Hofstede G: National cultures in four dimensions: a research-based theory of cultural differences among nations. Int Stud Man Org 1983; 8:46–74
6. Vingerhoets AJJM, Rottenberg J, Cevaal A, et al: Is there a relationship between depression and crying? a review. Acta Psychiatr Scand 2007; 115:340–351
7. Romans S, Clarkson R: Crying as a gendered indicator of depression. J Nerv Ment Dis 2008; 196:237–243
8. Beck AT, Ward CH, Mendelson M, et al: An inventory for measuring depression. Arch Gen Psychiatry 1961; 4:561–571
9. Gallagher D, Breckenridge J, Steinmetz J, et al: The Beck Depression Inventory and Research Diagnostic Criteria: congruence in an older population. J Consult Clin Psychol 1983; 51:945–946
10. Derogatis LR, Lipman RS, Covi L: SCL-90 : an outpatient psychiatric rating scale: preliminary report. Psychopharmacol Bull 1973; 9:13–28
11. Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62
12. Duda JE: History and prevalence of involuntary emotional expression disorder. CNS Spectrums 2007; 12(suppl 5):6–10
13. Parvizi J, Coburn KL, Shillcutt SD, et al: Neuroanatomy of pathological laughing and crying: a report of the American Neuropsychiatric Association Committee on Research. J Neuropsychiatry Clin Neurosci 2009; 21:75–87
14. Rottenberg J, Wilhelm FH, Gross JJ, et al: Vagal rebound during resolution of tearful crying among depressed individuals. Psychophysiology 2003; 40:1–6
15. Rabins PV, Arciniegas DB: Pathophysiology of involuntary emotional expression disorder. CNS Spectrums 2007; 12(suppl 5):17–22
16. Wortzel HS, Oster TJ, Anderson CA, et al: Pathological laughing and crying: epidemiology, pathophysiology, and treatment. CNS Drugs 2008; 22:531–545
17. Patel V: Crying behavior and psychiatric disorder in adults: a review. Compr Psychiatry 1993; 34:206–211
18. Udaka F, Yamao S, Nagata H, et al: Pathologic laughing and crying treated with levodopa. Arch Neurol 1984; 41:1095–1096
19. Moller M, Andersen G, Gjedde A: Serotonin 5-HT1A receptor availability and pathological crying after stroke. Acta Neurol Scand 2007; 116:83–90
20. Murai T, Barthel H, Berrouschot J, et al: Neuroimaging of serotonin transporters in post-stroke pathological crying. Psych Res Neuroim 2003; 123:207–211
21. Scoppetta M, Di Gennaro G, Scoppetta C: Selective serotonin reuptake inhibitors prevent emotional lability in healthy subjects. Eur Rev Med Pharmacol Sci 2005; 9:343–348
22. Nahas Z, Arlinghaua KA, Kotrla KJ, et al: Rapid response of emotional incontinence to selective serotonin reuptake inhibitors. J Neuropsychiatry Clin Neurosci 1998; 10:453–455
23. Polman CH, Reingold SC, Edan G, et al: Diagnostic criteria for multiple sclerosis: 2005 Revisions to the "McDonald Criteria." Ann Neurol 2005; 58:840–846
24. Miller DH, Weinshenker BG, Filippi M, et al: Differential diagnosis of suspected multiple sclerosis: a consensus approach. Mult Scler 2008; 14:1157–1174
25. Little JT, Ketter TA, Mathe A, et al: Venlafaxine but not bupropion decreases cerebrospinal fluid 5-hydroxyindoleacetic acid in unipolar depression. Biol Psychiatry 1999; 45:285–289
26. Moore AR, Gresham LS, Bromberg MB, et al: A self-report measure of affective lability. J Neurol Neurosurg Psychiatry 1997; 63:89–93
27. Feinstein A, Feinstein KJ, Gray T, et al: The prevalence and neurobehavioral correlates of pathological laughing and crying in multiple sclerosis. Arch Neurol 1997; 54:1116–1121
28. Hofstede G: Cultures and Organizations. Profile Books, Ltd, London, UK, 2003, p 84
29. Evans J, Platts H, Lightman S, et al: Impulsiveness and the prolactin response to d-fenfluramine. Psychopharmacology 2000; 149:147–152
30. Smith AG, Montealegre-Orjuela M, Douglas JE, et al: Venlafaxine for pathological crying after stroke. J Clin Psychiatry 2003; 64:731–732
31. Kim S-W, Shin I-S, Kim J-M, et al: Mirtazapine treatment for pathological laughing and crying after stroke. Clin Neuropharmacol 2005; 28:249–251
32. Ferentinos P, Paparrigopoulos T, Rentzos M, et al: Duloxetine for pathological laughing and crying. Int J Neuropsychopharmacol 2009; 12:1429–1430