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Seasonality of Cerebrospinal Fluid Monoamine Metabolite Concentrations and Their Associations with Meteorological Variables in Humans

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Abstract

Seasonal variations in neurotransmitter parameters have been previously reported in humans. However, these studies have involved small sample sizes and have not examined possible relationships with meteorological variables. We compared cerebrospinal fluid (CSF) concentrations of the major monoamine neurotransmitter metabolites (5-HIAA, HVA, and MHPG) in 188 healthy controls (80 men, 108 women) in relationship to age, sex, BMI, and available meteorological variables. All subjects had a lumbar puncture (LP) performed at 9 AM after overnight stay. Meteorological data for the *day prior* to LP were obtained from the National Climatic Association and included the photoperiod, percent sunshine, temperature (max, min, mean), barometric pressure, relative humidity, amount of precipitation and sky cover. Results revealed differences across seasons and cross-seasons for CSF 5-HIAA ($p < .05$), with post-hoc differences emerging between spring versus summer and fall and between x-spring and x-summer ($p < .05$). Differences were also found across seasons for CSF HVA ($p < .05$) with post-hoc differences between spring versus fall. CSF 5-HIAA was significantly inversely correlated with maximum ($r = -.28$, $p < 0.02$), minimum ($r = -.24$, $p < .04$), and mean temperature ($r = -.28$, $p < .02$) in men. In women, 5-HIAA ($r = -.22$, $p < .02$) and HVA ($r = -.28$, $p < .003$) were significantly correlated with relative humidity. These data confirm previous findings of variations in serotonin and dopamine metabolites across the year and highlight possible underlying mechanisms involving meteorological changes, which may result in alterations in neurophysiology and behavior.

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Keywords

cerebrospinal fluid; 5-hydroxyindoleacetic acid; homovanillic acid; seasonality; meteorological; temperature; relative humidity; sunshine

INTRODUCTION

Seasonal variations in central and peripheral neurotransmitter parameters have been previously reported in humans. In particular, significant seasonal variations in various parameters of serotonin (5-hydroxytryptamine, 5-HT) function have been noted and reviewed previously elsewhere (Brewerton, 1989). Seasonal variations in humans have been reported for cerebrospinal fluid (CSF) concentrations of serotonin (5-hydroxytryptamine, 5-HT) (Brewerton et al., 1995) and its major metabolite, 5-hydroxyindoleacetic acid (5-HIAA) (Brewerton et al., 1988; Luykx et al., 2012; Luykx et al., 2013), hypothalamic brain 5-HT (Carlsson et al., 1980), 5-HT transporter binding (Kalbitzer et al., 2010; Neumeister et al., 2000; Praschak-Rieder et al., 2008; Ruhe et al., 2009), plasma tryptophan availability (Maes, 1995), plasma 5-HT and 5-HIAA (Sarrias et al., 1989), platelet serotonin content (Brewerton et al., 1993; Wirz-Justice et al., 1977; Wirz-Justice and Richter, 1979), platelet 5-HT reuptake (Egrise et al., 1986; Marazziti et al., 1990), platelet ³H-imipramine binding (Arora and Meltzer, 1988; DeMet et al., 1989; Whitaker et al., 1984), ³H-paroxetine binding (Patkar et al., 2003), ³H-citalopram binding (Callaway et al., 2005), neuroendocrine responses to serotonergic agents (Brewerton, 1989; Brewerton et al., 1992).

Seasonal variation in various parameters of dopamine function have also been reported, including CSF concentrations of homovanillic acid (HVA) (Brewerton et al., 1988; Chotai and Åsberg, 1999), post-mortem brain dopamine (Karson et al., 1984), presynaptic dopamine synthesis (Eisenberg et al., 2010; Kaasinen et al., 2012), dopamine binding (Praschak-Rieder and Willeit, 2012), and blink rate (Karson et al., 1984).

Despite this seasonal variation in various serotonergic and dopaminergic parameters, their relationships with meteorological variables remains relatively unexplored. Phototherapy has been reported to not only alter serotonergic parameters but to also improve mood and reduce binge eating (Blehar and Rosenthal, 1989; Blouin et al., 1996; Braun et al., 1999; Harrison et al., 2015; Lam et al., 2016; Lambert et al., 2002; Szádóczy et al., 1989; Tyrer et al., 2016b). For this reason, it is often assumed that seasonal variations of biochemical parameters, including those involving central neurotransmitter functions, are a direct result of the effects of light. However, the effects of temperature and other meteorological variables have not often been factored into these analyses. Several investigators have reported ambient temperature effects on behaviors that may be influenced by monoamine neurotransmission, such as particular forms of violence (Anderson, 1989; Baron and Ransberger, 1978; Bushman et al., 2005; Lin et al., 2008; Maes et al., 1994; Michael and Zumpe, 1983, 1986; Qi et al., 2015; Vyssoki et al., 2012).

In this study, we assessed the association between cerebrospinal fluid (CSF) concentrations of the major monoamine neurotransmitter metabolites for serotonin (5-HIAA), dopamine (homovanillic acid, HVA), and norepinephrine (3-methoxy-4-hydroxyphenylglycol, MHPG)

and available meteorological variables in 188 healthy human subjects (80 = men, 108 = women). We hypothesized 1) seasonal and cross-seasonal variations in CSF monoamine metabolites, particularly 5-HIAA and HVA, and 2) that these seasonal/cross-seasonal variations will be associated with the meteorological variables at the time immediately prior to the lumbar puncture.(Brewerton et al., 1988; Karson et al., 1984).

CSF monoamine metabolites have previously been associated with differences in sex, age and body mass index (BMI), so we explored these variables initially to examine the relationships prior to assessing the impact of meteorological variables (Kusmierska et al., 2016; Markianos et al., 2013a; Markianos et al., 2013b; Williams et al., 2003). Higher CSF concentrations of 5-HIAA and HVA have been reported in females, in younger individuals, as well as in those with higher BMI's.

METHODS

Participants

One hundred eighty-eight healthy subjects were recruited as controls in a study of CSF variables in patients with affective illness and schizophrenia. Subjects were free of any major psychiatric disorder as determined by structured interview using the Schedule for Affective Disorders and Schizophrenia (Lifetime SADS) (Endicott, 1978). In addition, all subjects had complete medical and psychiatric histories, physical exams, and laboratory studies, including urine toxicology screens, prior to study.

Procedure

Subjects had a lumbar puncture (LP) performed at approximately 9 AM by one of the authors (SCR) on the Clinical Research Program's Inpatient Research Unit at the Emory University School of Medicine in Atlanta after overnight stay. Monoamine metabolite concentrations were determined by high-performance liquid chromatography (HPLC) with electrochemical detection (Scheinin et al., 1983). Further details regarding the methods are described elsewhere (Lewine et al., 1991; Risch et al., 1992). This study was approved by the Institutional Review Board of the Emory University School of Medicine and was conducted in accordance with the Helsinki Declaration.

Variables Studied—CSF monoamine concentrations were analyzed seasonally in two ways: The first method divided the data into four traditional seasons as defined by their solstices and equinoxes, i.e., winter = December 21 - March 20, spring = March 21 - June 20, summer = June 21 - September 20, and fall = September 21- December 20. The second method divided the data into four “cross-seasons” (x-seasons) (Brewerton, 1989; Brewerton et al., 1988). Cross-seasons (x-seasons) stagger the traditional seasons by half a season and are the quarters of the year that reflect the longest, shortest, and median periods of day length. For example, the x-season pivoting equally around the winter solstice (December 21) (“winter x-season”) is from November 6 through February 5 and includes the 3-month period with the shortest and narrowest range of the yearly photoperiod cycle as well as the least amount of cumulative yearly light. Likewise, the period of time pivoting around the summer solstice (June 21) (summer cross-season) is May 6 through August 5 and represents

the 3-month period with the longest and narrowest range of the yearly photoperiod cycle as well as the greatest amount of cumulative yearly light. The two cross-seasons pivoting about the spring (March 21) and autumn (September 21) equinoxes represent 3-month periods of the narrowest and most medial range of the yearly photoperiod cycle as well as essentially equal amounts of cumulative yearly light. However, the photoperiod is changing in opposite directions during these x-seasons.

In order to explore a possible causative role for weather, meteorological data for the *day prior* to LP were used in all analyses of weather effects, which included Pearson correlation coefficient determination and hierarchical regression. Meteorological data for the Atlanta area were obtained from the National Climatic Data Center of the National Oceanic and Atmospheric Administration (www.ncdcnoaa.gov) and included the following variables: temperature (TEMP) (MEAN, MINimum, MAXimum), relative humidity (RELHUM) (percent), barometric pressure (BAROPRES) (inches), precipitation (PRECIP) (inches), SUNSHINE (percent of total possible), degree of SKYCOVER (tenths: 0-10 scale), and photoperiod (PHOTOPER) (number of total minutes from sunrise to sunset),.

Statistics

Prior to examining the role of meteorological variables, the potential covariates, namely age, sex, education and BMI, that have been previously reported in the literature to contribute to the variance in CSF monoamine metabolites were examined using unpaired t-tests and Pearson “r” correlation coefficients. We found significant differences by sex in CSF 5-HIAA and HVA, but not MHPG. There were also significant differences in age between men and women, but not in BMI or education. Given these significant differences across sex, as well as the differences in sample sizes, correlations by sex using CSF monoamine metabolites and age, BMI and education were derived and reported in Table 1.

Metabolites were analyzed for seasons and x-seasons effects using ANCOVAs (covaried for age, sex, and BMI) and post-hoc least squares difference (LSD) t-tests (Brewerton, 1989; Brewerton et al., 1988). Next, hierarchical stepwise regression methods were performed to determine which factors (block 1 for demographic and block 2 for meteorological variables) significantly predicted each of the CSF monoamine metabolites (Tables 5–7). The Durbin-Watson statistic provided information if the assumption of independent errors was met. A value close to 2 for the Durbin-Watson means the assumption has been met for the regression model. Durbin-Watson value for the models reported in this study were acceptable range (1.79–2.16) to satisfy the assumption of independent errors. Multicollinearity, the correlation among independent variables, must always be considered when running regression models. The VIF is an indicator to assess multicollinearity, and model values between 1 and 10 mean there is no multicollinearity among predictor variables. The VIF values reported in this study ranged from 1.04-1.18 supporting independence among the predictor variables.

RESULTS

The mean age, BMI, years of education, and concentrations of monoamine metabolites of the subjects by sex are shown in Table 1. Women were significantly younger than the men

(33.0 ± 8.6 v. 36.3 ± 10.5 years, $p < .05$), and they also had significantly higher concentrations of 5-HIAA (99.4 ± 35.0 v. 79.4 ± 32.6 pmol/ml, $p < .001$) and HVA (181.4 ± 74.7 v. 151.6 ± 77.0 pmol/ml, $p < .001$).

After controlling for sex, age, BMI and education, results revealed significant differences across the seasons for CSF 5-HIAA ($F = 2.9$, $p < .05$) and HVA ($F = 3.26$, $p < .05$), but not MHPG, in the total group (see Table 2). Seasonal post-hoc comparisons revealed significant differences between spring and summer and spring and fall for both 5-HIAA and HVA. Significant differences were found across x-seasons for only 5-HIAA ($F = 3.33$, $p < .05$). Cross-seasonal post-hoc comparisons revealed significant differences between x-spring and x-fall for 5-HIAA ($F = 3.33$, $p < .05$).

Tables 3, 4 and 5 show the Pearson “r” correlation coefficients between CSF concentrations of monoamine metabolites and the demographic and meteorological variables in the total group, the men alone, and the women alone, respectively.

In the total group of subjects, there were significant positive correlations between 5-HIAA and age ($r = .15$, $p = .05$) and BMI ($r = .28$, $p = .001$), and significant negative correlations between 5-HIAA and RELHUM ($r = -.2$, $p = .007$), TEMP (MIN) ($r = -.2$, $p = .006$), TEMP (MEAN) ($r = -.18$, $p = .013$), and TEMP (MAX) ($r = -.15$, $p = .04$). There were also significant positive correlations between HVA and age ($r = .2$, $p = .007$) and BMI ($r = .28$, $p = .001$), as well as significant negative correlations between HVA and RELHUM ($r = -.26$, $p = .001$), TEMP (MIN) ($r = -.21$, $p = .005$), TEMP (MEAN) ($r = -.15$, $p = .014$), TEMP (MAX) ($r = -.15$, $p = .044$). Figures 1 and 2 show the plots between CSF 5-HIAA and HVA, respectively, and TEMP (MEAN). Figures 3 and 4 show the plots between CSF 5-HIAA and HVA, respectively, and RELHUM. Correlations between SUNSHINE and 5-HIAA ($r = .14$, $p = .07$) and HVA ($r = .13$, $p = .075$) were at a trend level. MHPG was significantly correlated with age ($r = .26$, $p = .001$), BMI ($r = .18$, $p = .015$), and years of education ($r = .18$, $p = .016$), but not with any of the meteorological variables.

In the men only, there were significant, positive correlations between BMI and 5-HIAA ($r = .37$, $p = .0001$), HVA ($r = .47$, $p = .0001$), and MHPG ($r = .21$, $p = .04$). There were significant, positive correlations between age and HVA ($r = .24$, $p = .011$) and MHPG ($r = .25$, $p < .008$) (see Table 4). Men also demonstrated a significant, positive correlation between age and 5-HIAA ($r = .24$, $p = .011$) and MHPG ($r = .25$, $p = .008$). There were negative correlations between 5-HIAA and TEMPAVG ($r = -.28$, $p = .02$), TEMPMAX ($r = -.28$, $p = .02$), and TEMPMIN ($r = -.24$, $p = .04$), and between HVA and RELHUM ($r = -.2$, $p = .085$). Neither CSF HVA nor MHPG were significantly correlated with any of the meteorological variables in the men.

In the women only, there were significant, positive correlations between BMI and 5-HIAA ($r = .37$, $p = .001$), HVA ($r = .47$, $p = .001$), and MHPG ($r = .21$, $p < .04$) (see Table 5). There were also significant, positive correlation between age and HVA ($r = .24$, $p = .011$) and MHPG ($r = .25$, $p = .008$). In addition, there were significant, positive correlations between percent sunshine and 5-HIAA ($r = .22$, $p = .025$) and HVA ($r = .19$, $p = .05$), and significant negative correlations between relative humidity and 5-HIAA ($r = -.22$, $p = .025$) and HVA ($r = -.22$, $p = .025$).

= $-.28$, $p < .003$), as well as between HVA and TEMPMIN ($r = -.2$, $p < .04$). MHPG was not significantly correlated with any of the variables studied in women.

Tables 6 and 7 show the results from hierarchical regression analyses in the total group for HIAA and HVA, respectively, using BMI, age, sex, and education as entered variables in step 1, and the following variables for *the day before the LP* entered in step 2: TEMP (MEAN, MIN, MAX), RELHUM (percent), BAROPRES (inches), PRECIP (inches), SUNSHINE (percent of total possible), degree of SKYCOVER (tenths: 0-10 scale), PHOTOPER (number of total minutes from sunrise to sunset).

For HIAA (Table 6), after controlling for BMI, age, sex and education, the only meteorological variable that was a statistically significant predictor was mean temperature. Model 2 predicted 28% of the variance ($R = .53$, $R^2 = .284$, Adjusted $R^2 = .254$, $F = 9.66$, $p < .0001$). Mean temperature accounted for an additional 3% of the variance in predicting HIAA after controlling for the demographic variables in model 1.

For HVA (Table 7), relative humidity was a statistically significant predictor, and together with the demographic variables, Model 2 predicted 22% of the variance ($R = .474$, $R^2 = .224$, Adjusted $R^2 = .193$, $F = 7.1$, $p < .0001$). The addition of the meteorological variable of relative humidity explained an additional 7% of the variance for HVA after controlling for the demographic variables in model 1.

For MHPG, the demographics alone (model 1) predicted 12% of the variance ($R = .346$, $R^2 = .12$, Adjusted $R^2 = .091$, $F = 4.19$, $p < .003$), and none of the meteorological variables significantly accounted for the variance in MHPG.

DISCUSSION

These data confirm previous findings of statistically significant variations in serotonin and dopamine metabolites across the year and highlight possible underlying mechanisms involving a complex interplay of the amount of available sunshine, ambient temperature, relative humidity, age, gender, and BMI. The effects of light and temperature on 5-HIAA and HVA appear to be in opposite directions in that their correlations with sunshine are positive, and their correlations with temperature and relative humidity are negative, although these associations appear to be somewhat gender-specific. Correlations between temperature and 5-HIAA were only statistically significant in men, while significant correlations between relative humidity and amount of sunshine and both 5-HIAA and HVA were only found in women. The reasons for these apparent gender differences in sensitivity to meteorological variables are unknown. However, the linear regression results suggest that the temperature and relative humidity effects on 5-HIAA and HVA are stronger than that of the amount of available sunshine or the photoperiod itself.

The extent to which changes in the weather result in alterations in behavior remains to be further investigated, but our results strongly suggest that such weather effects may be mediated by alterations in monoamine function, particularly that of serotonin and dopamine. Both light and temperature are known to affect 5-HT function. In animals, light has been reported to rapidly and significantly increase 5-HT neuronal reactivity and sensitivity

(Cagampang et al., 1993; Mason, 1988). Increasing the photoperiod has also been reported to significantly increase both platelet [3H]-imipramine binding and 5-HT uptake in rat hypothalami (Rovescalli et al., 1989). In patients with seasonal affective disorder (SAD) there are significantly different prolactin responses following m-chlorophenylpiperazine (m-CPP) before and after phototherapy (Garcia-Borreguero et al., 1995). Serotonin's role in thermoregulation is well established (Lin, 1978), and it is known that temperature significantly affects serotonin function *in vitro* (Bley et al., 1994; Skeen et al., 1992). The effects of ambient temperature on central serotonin function *in vivo* are less well understood, but available evidence in animals suggests that high ambient temperatures cause increases in plasma, hypothalamic, and brain 5-HT and also enhance 5-HT₂ receptor sensitivity (Chiu et al., 1995; Sharma and Hoopes, 2003; Zhang and Tao, 2011).

These results may be relevant to several reports in the literature regarding seasonal variations in psychiatric symptoms or behaviors related to monoaminergic dysfunction. Serotonin dysfunction has been linked to affective, anxiety and eating disorders, as well as migraine, all of which have been reported to have seasonal variations in symptoms (Brewerton, 1989; Brewerton, 1995; Brewerton and George, 1990; Brewerton and Jimerson, 1996; Hardin et al., 1991; Marazziti, 2017). In addition, behaviors connected to 5-HT dysfunction include certain forms of violence and impulsive behaviors, including suicide, homicide, sexual assault, and arson (Christodoulou, C. et al., 2012; Christodoulou, C. et al., 2012; Christodoulou et al., 2017; Christodoulou et al., 2009; Kattimani et al., 2016; Nader et al., 2011; Postolache et al., 2010; Vyssoki et al., 2012; White et al., 2015; Woo et al., 2012). Temperature has been reported to be significantly correlated to violent behavior, including assaults against women and suicides, especially by violent means (Anderson, 1989; Bushman et al., 2005; Cohn, 1990; Maes et al., 1993; Maes et al., 1994; McCleary et al., 1991; Michael and Zumpe, 1983, 1986; Rotton and Frey, 1985). Binge and purge behavior has been correlated with the photoperiod (Blouin et al., 1992). It is important to note that temperature and the photoperiod are highly correlated with each other, so unless both of these parameters are studied simultaneously, it is impossible to sort out their differential effects on behavior.

Further studies are needed to explore the relationships between various aspects of the weather, such as temperature and relative humidity, and central monoamine function, particularly that of serotonin and dopamine.

Strengths of this study include the fact that all controls were carefully screened for medical and psychiatric illness, and all lumbar punctures were performed by the same investigator and co-author (SCR) in the same place at the same time of day, and our sample size was adequate. In addition, we controlled for demographic factors including sex, age, BMI, and years of education, as well as for meteorological variables measured on the day prior to LP. No previous study to our knowledge has evaluated all of these variables in the same study.

There are several limitations of this study. This is a cross-sectional sample of CSF samples collected only once from different subjects at different times of the year. An ideal study would collect samples from the same individuals several times over the course of multiple years to better control for individual and seasonal differences, although the feasibility and

ethics of such a study are questionable. In addition, given that the 5-HTTLPR short allele has been associated with larger seasonal fluctuations in brain serotonin function and increased responsiveness to climatic variables and other environmental influences, it would have been of interest to investigate whether 5-HTTLPR genotype influenced our results (Luykx et al., 2013). However, no genotyping was done in this study. Another limitation is that no behavioral data was assessed on the day of lumbar puncture.

Although we are unable to conclude that meteorological variables actually cause changes in monoamine metabolite levels and hence, monoamine function, our analyses use meteorological variables observed the day prior to the LP, and therefore the meteorological changes came prior to obtaining the CSF. Although the time relationship between a shift in weather variables and a change in individual biochemistry in humans remains to be determined, increasing ambient temperature and light in animals results in rapid changes in the serotonergic system (Cagampang et al., 1993; Chiu et al., 1995; Mason, 1988; Sharma and Hoopes, 2003). These changes may be relevant to the various serotonin-associated behaviors reported in clinical and non-clinical populations (Alstadhaug et al., 2007; Blouin et al., 1992; Brewerton, 1989; Brewerton, 2001; Brewerton and Ballenger, 1992; Brewerton and George, 1990; Coimbra et al., 2016; Hardin et al., 1991; Makris et al., 2016; Michael and Zumpe, 1983; Postolache et al., 2010; Prashak-Rieder and Willeit, 2012; Tyrer et al., 2016a). Another limitation of this study is that we only analyzed data from the day prior to the LP. We acknowledge that lagged correlations and moving averages of variables collected on multiple days prior to LP are needed to establish the best predictor.

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Figure 1.

Plot of CSF 5-HIAA versus mean temperature (TEMP (MEAN)) in the total group of healthy men (squares) and women (circles) ($n=188$) ($r = -.18$, $p = .01$).

Figure 2.
Plot of CSF HVA versus mean temperature (TEMP (MEAN)) in the total group of healthy men (squares) and women (circles) (n=188) ($r = -.18$, $p = .01$).

Figure 3.

Plot of CSF 5-HIAA versus relative humidity (RELHUM) in the total group of healthy men (squares) and women (circles) (n=188) ($r = -.2$, $p = .007$).

Figure 4.

Plot of CSF HVA versus relative humidity (RELHUM) in the total group of healthy men (squares) and women (circles) (n=188) ($r = -.26$, $p = .001$).

Table 1

Mean ($\pm$ SD) age, BMI, years of education, and CSF concentrations of 5-HIAA, HVA and MHPG in healthy controls by sex.

	Men (n=78)	Women (n=110)	t-value
Age	33.0 $\pm$ 8.6 years	36.3 $\pm$ 10.5 years	-2.46 *
BMI	24.9 $\pm$ 3.1	23.9 $\pm$ 4.4	1.9
Education	15.4 $\pm$ 2.5 years	14.7 $\pm$ 2.9 years	1.64
5-HIAA (pmol/ml)	79.4 $\pm$ 32.6	99.4 $\pm$ 35.0	-3.94 ***
HVA (pmol/ml)	151.6 $\pm$ 77.0	181.4 $\pm$ 74.7	-2.64 **
MHPG (pmol/ml)	42.1 $\pm$ 8.6	41.0 $\pm$ 7.9	.35

= p < .001,

*
= p < .05

Mean ($\pm$ SD) concentrations of 5-HIAA, HVA and MHPG in healthy controls by season and cross-season (x-season) covaried by age, sex, and BMI (* = $p < .05$). Significant post-hoc comparisons (least squares difference) are indicated by different letters ($p < .05$).

Table 2

	Winter (n = 22)	Spring (n = 44)	Summer (n = 61)	Fall (n = 46)	F-Value
HIAA	93.4 $\pm$ 28.7	102.8 $\pm$ 37.7 ^a	84.8 $\pm$ 34.0 _b	87.5 $\pm$ 35.5 ^b	2.9*
HVA	190.3 $\pm$ 73.5	193.5 $\pm$ 77.7 ^a	149.5 $\pm$ 68.0 ^b	163.2 $\pm$ 84.5 ^b	3.26*
MHPG	41.4 $\pm$ 7.8	40.7 $\pm$ 6.5	42.1 $\pm$ 9.9	41.5 $\pm$ 7.9	2.76
	X-Winter (n = 30)	X-Spring (n = 41)	X-Summer (n = 40)	X-Fall (n = 53)	F-Value
HIAA	96.3 $\pm$ 36.6	105.0 $\pm$ 38.4 ^a	81.4 $\pm$ 33.1	86.7 $\pm$ 31.0 ^b	3.33*
HVA	184.5 $\pm$ 97.3	192.2 $\pm$ 77.7	158.7 $\pm$ 73.3	153.4 $\pm$ 63.8	2.09
MHPG	40.1 $\pm$ 8.3	41.4 $\pm$ 6.8	40.7 $\pm$ 8.7	43.2 $\pm$ 8.9	2.05

Table 3

Pearson “r” correlation coefficients of CSF monoamine concentrations with demographic variables and meteorological measures on day before LP in total group of healthy men and women (n=188).

	5-HIAA	HVA	MHPG
Age (years)	.15 [*]	.2 ^{**}	.26 ^{***}
BMI (kg/m ²)	.28 ^{***}	.28 ^{***}	.18 [*]
Education (years)	-.06	-.09	.18 [*]
TEMP (MEAN)	-.18 ^{**}	-.18 ^{**}	.00
TEMP (MIN)	-.2 ^{**}	-.21 ^{**}	-.004
TEMP (MAX)	-.15 [*]	-.15 [*]	.02
RELHUM (%)	-.2 ^{**}	.26 ^{***}	-.03
PRECIP (inches)	-.08	-.09	.02
SUNSHINE (% of total)	0.14 ⁺	0.13 ⁺	.04
SKYCOVER (tenths)	-.06	-.09	-.05
BAROPRES (inches Hg)	-.03	.06	0.02
PHOTOPER (minutes)	.11	.1	.04

= p .001,

**
= p .01,

*
= p .05,

⁺
= p .075

Table 4

Pearson “r” correlation coefficients of CSF monoamine concentrations with demographic variables and meteorological measures on day before LP in men only (N=78).

	5-HIAA	HVA	MHPG
Age (years)	.13	.06	.31 **
BMI (kg/m ²)	.32 **	.04	.13
Education (years)	-.16	-.1	-.03
TEMP (MEAN)	-.028 *	-.17	-.01
TEMP (MIN)	-.24 *	-.17	-.01
TEMP (MAX)	-.28 *	-.18	-.01
RELHUM (%)	-.1	-.02 +	.09
PRECIP (inches)	-.1	-.05	.002
SUNSHINE (% of total)	-.01	.03	-.04
SKYCOVER (tenths)	.06	.11	.11
BAROPRES (inches Hg)	.04	.02	-.02
PHOTOPER (minutes)	-.1	-.01	-.04

= p .001,

**
= p < .01,

*
= p .05,

+
= p .1

Table 5

Pearson “r” correlation coefficients of CSF monoamine concentrations with demographic variables and meteorological measures on day before LP in women only (N=110).

	5-HIAA	HVA	MHPG
Age (years)	.1	.24 *	.25 **
BMI (kg/m ²)	.37 ***	.47 ***	.21 *
Education (years)	.03	-.06	.3 **
TEMP (MEAN)	-.08	-.15	-.003
TEMP (MIN)	-.13	-.2 *	-.01
TEMP (MAX)	-.04	-.1	-.02
RELHUM (%)	-.22 *	-.28 **	-.11
PRECIP (inches)	-.04	-.11	-.02
SUNSHINE (% of total)	.22 *	.19 *	.1
SKYCOVER (tenths)	-.15	-.17	-.08
BAROPRES (inches Hg)	-.07	.07	-.02
PHOTOPER (minutes)	-0.03	-.13	.08

= p .001,

**
= p < .01,

*
= p .05,

+
= p < .1

Table 6

Prediction models for HIAA using backwards stepwise linear regression.

		<i>b</i>	<i>SE b</i>	<i>B</i>
HIAA				
Step 1	Constant	−40.49	26.9	
	BMI ***	3.59	.79	.37
	Age	.05	.32	.01
	Sex ***	28.94	6.15	.39
	Education	−.17	1.04	−.01
Step 2	Constant	−8.51	29.9	
	BMI ***	3.5	.78	.36
	Age	.02	.31	.005
	Sex ***	27.54	6.08	.37
	Education	−.17	1.04	−.01
	Temperature (mean) *	−.48	.21	−.18
All other meteorological variables failed to reach significance				

Note:

* $p < .05$,

** $p < .01$,

*** $p < .001$

Table 7

Prediction models for HVA using backwards stepwise linear regression.

		<i>b</i>	<i>SE b</i>	<i>B</i>
HVA				
Step 1	Constant	−48.43	61.33	
	BMI **	5.67	1.81	.28
	Age	.84	.73	.1
	Sex **	40.51	14.01	.25
	Education	−.9	2.36	−.03
Step 2	Constant	114.39	77.31	
	BMI *	4.54	1.78	.22
	Age	.92	.7	.11
	Sex *	33.77	13.65	.21
	Education	−1.3	2.28	−.05
	Relative humidity ***	−1.49	.45	−.27
All other meteorological variables failed to reach significance				

Note:

* $p < .05$,

** $p < .01$,

*** $p < .001$