CSF Oxytocin and Vasopressin Levels after Recovery from Bulimia Nervosa and Anorexia Nervosa, Bulimic Subtype

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Background: When ill, people with eating disorders have disturbances of the neuropeptides vasopressin and oxytocin.

Methods: To avoid the confounding effects of the ill state, we studied women who were recovered (more than 1 year, normal weight, and regular menstrual cycles, no bingeing or purging) from bulimia nervosa (rBN) or binge eating/purging–type anorexia nervosa (rAN-BN), and matched healthy control women.

Results: Vasopressin was elevated in rAN-BN and showed a trend towards elevation in rBN. In rBN, elevated cerebrospinal fluid vasopressin may be related to having a lifetime history of major depression. In comparison, cerebrospinal fluid oxytocin was normal in recovered subjects, but elevated levels in some rBN might be related to birth control pill use.

Conclusions: These data confirm and extend the possibility that elevated cerebrospinal fluid vasopressin may be related to the pathophysiology of eating disorders, and/or a lifetime history of major depression.

Key Words: Anorexia nervosa, bulimia nervosa, oxytocin, vasopressin, major depression, obsessive–compulsive disorder

Introduction

Bulimia nervosa (BN), a disorder of unknown etiology that has its onset in young women, is characterized by binge eating followed by compensatory methods to prevent weight gain (American Psychiatric Association 1994). Most commonly, women with BN maintain a normal weight. Bulimic symptoms also occur less commonly in people with the binge eating/purging type of anorexia nervosa (AN-BN). People who are ill with BN and AN-BN have a similar range of comorbid symptoms (Garfinkel et al 1995) and a wide variety of neuroendocrine disturbances (Kaye et al 1998a), which could be a consequence of central nervous system neuropeptide dysregulation. For example, altered concentrations of oxytocin (OXT) and vasopressin (AVP) have been found in people with eating disorders (EDs) (Demitrack et al 1990, 1992; Gold et al 1983a).

OXT and AVP are produced in the hypothalamic supraoptic and paraventricular nucleus and are released peripherally via pituitary projections to the neurohypophysis, and also centrally directed into the brain (Swaab et al 1993). Central and peripheral OXT and AVP are independently regulated (Geiner et al 1988), with the peripheral activities of these peptides best known. AVP controls free-water clearance of the kidney, whereas OXT promotes uterine contraction and milk let-down. In the brain, these peptides are long-acting neuromodulators and exert complex behavioral effects. OXT administration to rats disrupts memory consolidation and retrieval, whereas AVP administration enhances memory function. In animal models, OXT has anxiolytic actions, whereas AVP has anxiogenic effects (Liebsch et al 1996; McCarthy et al 1995). Thus, in several ways the effects of OXT appear to be reciprocal to the effects of AVP. In terms of EDs, these neuropeptides are of interest because they influence feeding behavior (Burlet et al 1990; Olson et al 1991) and have also been implicated in obsessional behaviors (Leckman et al 1994) and depression (Gjerris et al 1985).

It is not known whether alterations in OXT or AVP are a consequence of pathologic eating or malnutrition, or if they are premorbid traits that contribute to a vulnerability to develop EDs. Determining whether abnormalities are a consequence or a potential antecedent of pathological feeding behavior is a major question in the study of EDs. It is impractical to study people with EDs prospectively, because of the young age of onset and difficulty in premorbid identification of people who will develop this illness. Therefore, we studied women who were recovered for more than a year from BN or AN-BN. Any persistent psychobiological abnormalities might be trait-related and might potentially contribute to the pathogenesis of the disorders.
Subjects had to maintain a body weight of >90% average body weight (%ABW) (Metropolitan Life Insurance Company 1959), have regular menstrual cycles; have not binged, purged, or engaged in restrictive eating patterns; and have not met criteria for substance-related disorders. None of the subjects had a current major depressive episode. Current depressive symptoms were assessed with the Hamilton Depression Rating Scale (HDRS; Hamilton 1967) and current obsessive and compulsive symptoms with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al 1989). All subjects completed a 7-day diary at home, in which they listed individual food items consumed, portion sizes, and exercise frequency. This information was used to confirm the presence of relatively normal dietary intake. Subjects were free of medication for 6 weeks prior to the study and gave informed consent.

A lumbar puncture (LP) for obtaining cerebrospinal fluid (CSF) samples without preservative was performed during the early follicular phase by methods previously described (Kaye et al 1998b). CSF OXT and AVP assays were performed by radioimmunoassay also as previously described (Altemus et al 1994). A modified version of the Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L) was used for assessment of lifetime axis I diagnoses (Kaye et al 1998b). Three NC, two rAN-BN, and nine rBN women were taking birth control pill (BCP) at the time of the study.

One-way analysis of variance (ANOVA) and Tukey’s post hoc test were used to investigate three group comparisons. Analysis of covariance (ANCOVA) was applied for confounding variables. Two-way ANOVA investigated possibly interacting independent within-group factors when all cells were filled; otherwise stepwise regression was applied. Correlations were assessed by Spearman correlation coefficients. For statistical analyses, the SPSS (Chicago) software package was used (Barcikowski 1984).

Methods and Materials

Thirty-three women who had previously met DSM-IV criteria for an ED were recruited: 23 women recovered from BN (rBN), and 10 subjects recovered from binge/purging–type AN (rAN-BN). The rBN women had never had AN. Recovered ED subjects were compared to 17 female normal control subjects (NC), who were recruited through advertisements in local newspapers and who were without lifetime psychiatric or major medical illnesses. In the year before the study, all participating subjects had to maintain a body weight of >90% average body weight (%ABW) (Metropolitan Life Insurance Company 1959), have regular menstrual cycles; have not binged, purged, or engaged in restrictive eating patterns; and have not met criteria for substance-related disorders. None of the subjects had a current major depressive episode. Current depressive symptoms were assessed with the Hamilton Depression Rating Scale (HDRS; Hamilton 1967) and current obsessive and compulsive symptoms with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al 1989). All subjects completed a 7-day diary at home, in which they listed individual food items consumed, portion sizes, and exercise frequency. This information was used to confirm the presence of relatively normal dietary intake. Subjects were free of medication for 6 weeks prior to the study and gave informed consent.

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Table 1. Comparison of Study Subjects on Demographic Variables and Cerebrospinal Fluid Oxytocin and Vasopressin

<table>
<thead>
<tr>
<th></th>
<th>Recovered normal weight bulimics (n = 23)</th>
<th>Recovered binge eating/purging-type anorexics (n = 10)</th>
<th>Normal control women (n = 17)</th>
<th>F (df = 2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.4 ± 6.2</td>
<td>25.9 ± 3.2</td>
<td>23.4 ± 4.4</td>
<td>1.8</td>
<td>.18</td>
</tr>
<tr>
<td>% average body weight (%ABW)</td>
<td>111 ± 10°</td>
<td>101 ± 10°</td>
<td>105 ± 7.5</td>
<td>4.9</td>
<td>.01</td>
</tr>
<tr>
<td>Maximum lifetime %ABW</td>
<td>123 ± 11°</td>
<td>120 ± 19</td>
<td>110 ± 9°</td>
<td>5.5</td>
<td>.00</td>
</tr>
<tr>
<td>Minimum lifetime %ABW</td>
<td>95 ± 8°</td>
<td>69 ± 8°</td>
<td>96 ± 8°</td>
<td>43.3</td>
<td>.00</td>
</tr>
<tr>
<td>Age of onset of eating disorder (years)</td>
<td>16.2 ± 3</td>
<td>14.8 ± 2.4</td>
<td>—</td>
<td>1.6</td>
<td>.22</td>
</tr>
<tr>
<td>Length of recovery (months)</td>
<td>38.7 ± 25</td>
<td>26.8 ± 19</td>
<td>—</td>
<td>1.8</td>
<td>.19</td>
</tr>
<tr>
<td>Hamilton Depression Rating Scale</td>
<td>7.4 ± 6.6 (18)</td>
<td>7.9 ± 4.8 (9)</td>
<td>4.1 ± 3.6 (14)</td>
<td>4.5</td>
<td>.15</td>
</tr>
<tr>
<td>Yale Brown Obsessive Compulsive Scale</td>
<td>9.4 ± 7.4° (18)</td>
<td>9.6 ± 7.6° (9)</td>
<td>2.6 ± 3.8° (14)</td>
<td>5.2</td>
<td>.01</td>
</tr>
<tr>
<td>Oxytocin pmol/L</td>
<td>6.37 ± 1.79</td>
<td>7.32 ± 2.22</td>
<td>6.26 ± 1.95</td>
<td>1.1</td>
<td>.35</td>
</tr>
<tr>
<td>Vasopressin pmol/L</td>
<td>0.74 ± 0.20</td>
<td>0.89 ± 0.17°</td>
<td>0.66 ± 0.13°</td>
<td>5.3</td>
<td>.01</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

p < .05 for *a* vs. *b* (Tukey’s post hoc test).

Results

The three subject groups (Table 1) were of similar ages. Current %ABW was lower in rAN-BN compared to rBN women, and as expected, there were significant differences in high and low lifetime %ABW. ED subjects had a similar age of onset of their ED.

The three subject groups had similar CSF OXT values; however, CSF AVP concentrations were significantly elevated in the rAN-BN compared to NC, and tended to be higher compared to rBN women (p = .06, Tukey’s post hoc test). When the three groups were combined, age was significantly associated with CSF AVP (r = .43, p < .05). Separate ANCOVAs with age as covariate showed that CSF AVP in the rAN-BN was significantly higher than for NC subjects [F(1) = 12.1, p < .002], or rBN [F(1) = 6.2, p < .02].

A series of exploratory analyses was done in rBN subjects to determine whether depression or obsessive–compulsive disorder (OCD) or other factors were related to neuropeptide levels. The rAN-BN group was not analyzed because of their small cell sizes. rBN with a lifetime history of OCD had higher CSF OXT concentrations (n = 5, 7.74 ± 2.0 pmol/L) than did rBN subjects without a lifetime OCD diagnosis (n = 16, 5.89 ± 1.6 pmol/L, p = .05). In addition, rBN with a lifetime history of major depressive disorder (MDD) had higher CSF AVP concentrations (n = 17, 6.50 ± 2.0 pmol/l) than did rBN without a lifetime MDD diagnosis (n = 4, 5.63 ± 1.2 pmol/l, p = .03). Neither CSF AVP or OXT was related to current depression or OCD symptoms in rBN. To determine whether BCP use contributed to these findings, a stepwise regression analysis was done. This showed that elevated CSF OXT in rBN was mainly related to BCP.
intake ($t = 3.2, p = .005$) but not to a lifetime history of lifetime OCD ($t = 1.1, p = .3$); however, birth control use had no effect on CSF AVP ($t = 0.87, p = .40$) as the relationship of CSF AVP and a history of MDD ($t = 2.28, p = .03$) remained significant.

**Discussion**

These data confirm and extend the possibility that long-term, recovered eating disorder subjects with bulimic-type symptoms have increased CSF AVP. Previous studies (Demitrack et al 1990; Gold et al 1983a) found elevated CSF AVP levels in ill and recovered subjects with eating disorders but subgrouping by types of eating behavior was not done. This study raises the possibility that elevated CSF AVP is particularly associated with depressive symptoms. Such questions were not asked in previous studies of people with eating disorders. The small size of subject groups after segregating by ED type and Axis I diagnosis limits our power to investigate the interactions of these diagnoses and AVP. Other studies have found elevated CSF AVP in people with lifetime MDD who were not currently depressed (Sorensen et al 1986), whereas other studies suggest reduced CSF AVP levels in depression (Gold et al 1983b). We also found that CSF AVP was associated with age. We are not aware of a study in humans investigating age as a covariate for this peptide; however, age was related to the circadian pattern of CSF AVP in an animal study (Jolkkonen et al 1986).

As a group, recovered subjects had normal CSF OXT levels. These data, however, raise a question of whether CSF OXT is related to a lifetime history of OCD or BCP use. CSF OXT has not been previously measured in recovered ED subjects. People with OCD have been reported to have both normal (Altemus et al 1999) and elevated levels of CSF AVP in an animal study (Jolkkonen et al 1986). In terms of limitations, the small size of the recovered ED groups makes segregation by diagnosis or BCP problematic. Thus, these preliminary data raise interesting questions, but replication is needed in a larger sample.

**References**


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