Interrelationships Among Anxiety, Aggression, Impulsivity, and Mood: A Serotonergically Linked Cluster?

Alan Apter, Herman M. van Praag, Robert Plutchik, Serge Sevy, Martin Korn, and Serena-Lynn Brown

Abstract. Serotonin abnormalities appear to be related to a variety of psychopathological dimensions such as anxiety, depressed mood, impulsivity, and aggression dysregulation. We hypothesized that the psychopathological dimensions related to serotonin would be significantly intercorrelated since they seem to have a common biological basis. Sixty psychiatric inpatients were examined on a series of psychometric tests measuring suicidality, violence potential, impulsivity, depressive mood, and anxiety. The scores on all of these measures tended to be significantly correlated with one another. These findings support the additional hypothesis that biological markers may be more closely related to basic psychological dimensions than to nosological categories.

Key Words. Serotonin, psychiatric inpatients, psychometric tests, depression, violence, suicidality.

Abnormalities of serotonin (5-hydroxytryptamine, 5HT) metabolism were initially reported in depression but were later found in a wide variety of psychiatric conditions, including anxiety states, schizophrenia, obsessive-compulsive disorders (OCD), and alcoholism. The increasing number of psychiatric states in which 5HT metabolism is found to be disturbed has led some investigators to the conclusion that 5HT is a nonspecific “transmitter for all seasons” (van Kammen, 1987). This view has recently been challenged by van Praag et al. (1987), who point out that although 5HT abnormalities cut across nosological boundaries, this does not necessarily imply a lack of specificity. They argue instead that 5HT may be related to some basic psychopathological dimensions that are associated with depression but are not specific to depressive disorder.

Various investigations have indicated that low levels of 5-hydroxyindolacetic acid (5HIAA) in cerebrospinal fluid (CSF) characterize those depressives who have been violently suicidal (Åsberg et al., 1976; Ågren, 1980; Oreland et al., 1981; van Praag, 1982; Banki and Arató, 1983; Palaniappan et al., 1983; Banki et al., 1984; Lopez-Iboret...
al., 1985). In addition, this association cuts across diagnostic entities and is found both in nondepressed, nonpsychotic suicide attempters (Oreland et al., 1981; Träskman et al., 1981; Banki and Arató, 1983) and schizophrenic suicide attempters (van Praag, 1983; Ninan et al., 1984). Low CSF 5HIAA is also found in subjects who are outwardly aggressive without being suicidal (Brown et al., 1979, 1982; Linnoila et al., 1982; Lidberg et al., 1984; Brown and Goodwin, 1986; Virkunnen et al., 1987). Thus, it seems that low CSF 5HIAA tends to be associated with aggressive behavior irrespective of diagnosis and direction of the aggression. On the basis of this evidence, van Praag et al. (1987) hypothesized that low CSF 5HIAA is a correlate of a basic psychological dysfunction (i.e., aggression dysregulation) rather than of a particular nosological entity (e.g., depressive disorder). It is conceivable that the 5HT disturbance found in OCD (Insel et al., 1985; Zohar and Insel, 1985) relates to the aggression dysregulation that often features prominently in this disorder. Studies to examine this issue, however, have not been performed.

It is only comparatively recently that psychometricians have begun to take an interest in the dimension of impulsivity (Lorr and Wunderlich, 1985). There is now good evidence that impulsivity is a basic psychological trait with an important heritable component (Roy, 1983; Plutchik and van Praag, 1986). Impulsivity has also been suggested as the underlying dysfunction to which low CSF 5HIAA in suicidal and violent patients is related (Linnoila et al., 1982; Lidberg et al., 1985; van Praag, 1990). Plutchik et al. (1986) have shown that psychometric measures of impulsivity correlate significantly with psychometric measures of suicide and violence risk.

Furthermore, depressed mood has been postulated to be related to 5HT dysfunction (van Praag et al., 1987), since normal volunteers may show depressive features on low tryptophan diets (Young et al., 1987) and depressive patients who responded to antidepressants seem to relapse on such a diet (Charney et al., 1988). The observation that CSF 5HIAA is lower in depressed patients who have made a suicide attempt than in nondepressed suicide attempters (Träskman et al., 1981) points in the same direction.

In addition to aggression dysregulation, impulsivity, and depressed mood, a fourth psychological variable has been associated with 5HT dysfunction—anxiety. The biochemical evidence for this has recently been extensively reviewed by Kahn et al. (1988) and van Praag et al. (1987). Clinical observers have pointed out that depressed mood, anxiety, and aggression tend to cluster (Kahn et al., 1988). Panic disorder and OCD, for example, are frequently accompanied by major depression, and depressed patients have an increased tendency to panic attacks, generalized anxiety, and obsessive-compulsive symptoms. Similarly, depression and aggression are linked, since depressed patients show not only increased suicidality but also have very high hostility and aggression ratings (Farmer, 1987).

Thus, the psychopathological dimensions that have been associated with 5HT dysfunction include anxiety, impulsivity, depressed mood, suicide, and violence (Brown et al., 1982; Plutchik and van Praag, 1986; van Praag et al., 1987). In this study, our hypothesis was that these psychopathological dimensions would show a high intercorrelation as they all seem to be related to a similar biochemical system.
Methods

Subjects. Sixty patients on the acute psychiatric inpatient wards of the Bronx Municipal Hospital Center were interviewed and tested. The semistructured interview took place within 10 days of admission to the inpatient service. The selection of patients was random subject to some restrictions. Patients who were not eligible for this study were those under 18 years of age or over 64 years of age, those with organic syndromes, or those with a lack of fluency in English. Both the patients and the patients' therapists had to agree to the patients' participation. No attempt was made to select any particular diagnostic category of patients since our departure point was a dimensional one (van Praag et al., 1987), and clinical experience indicates that the dimensions to be investigated occur in all diagnostic categories.

Almost all patients were on medications. A survey of medication use indicated that 25% of the patients were on antianxiety drugs, 6% were on antidepressants, and about 50% were on neuroleptics. Although these medications may have some effects on serotonin levels, the fact that patients were tested early in their hospital stay would suggest that medication effects were relatively minimal.

Patients were selected for the study if the reason for admission was a suicide attempt. For each such patient, a nonsuicidal control patient was selected and matched for sex, age, and diagnosis. Thus, there were 30 patients who had been admitted for a suicide attempt and 30 patients who had been admitted for other reasons. A suicide attempt was defined as a life-threatening action made by the patient against himself or herself, this action being serious enough to warrant admission. There were 15 males and 15 females in each group; the mean age of the suicidal patients was 29 (SD = 9.5) years and of the nonsuicidal patients was 32.5 (SD = 10.8). Seventeen of each group were diagnosed as having a personality disorder, six of each group had schizophrenia, and seven of each group had a major depressive disorder. In addition, followup on the ward found that 20 patients had to be secluded or restrained for assaulting a staff member or another patient. This group was compared to the group of patients who were not violent on the ward. Only two of the violent patients had not been admitted for a suicide attempt.

Assessment Interview. Each patient was interviewed by an experienced psychiatrist about the reason for admission and the events leading up to the suicidal act, if such an attempt had taken place. All patients were interviewed within 1 week of admission. On the basis of this interview, a chart review, and a discussion with the ward psychiatrist, the research team then placed the patients in one of the following three broad diagnostic categories: schizophrenia, major affective disorder, and personality disorder. Diagnoses were made according to DSM-III-R criteria (American Psychiatric Association, 1987). A battery of self-report test measures was administered. The psychiatrist was present with the patient at all times and, if requested, would read the questions and record the patient's answers.

Assessment Instruments.

Suicide risk. The Suicide Risk Scale consists of 26 items answered by the patient as yes or no. They include items on past history of suicide attempts, present strength of suicidal impulses, feelings of depression and hopelessness, and other items that have been reported to be associated with patients who have made suicide attempts (Conte and Plutchik, 1974). Such items include frequent use of tranquilizers, sleeping pills, and medications of all types.

The internal reliability (coefficient α) of the scale has been found to be 0.84, indicating high intercorrelations among the items. The scale has been given to psychiatric outpatients and inpatients. It correlates with clinicians' judgments of suicidal risk in patients as well as with outcome measures of outpatient psychotherapy. Scores on the Suicide Risk Scale discriminated between a group of outpatients clinically evaluated as having suicidal symptoms and a group of patients who had no suicidal symptoms. It also discriminated between inpatients who had made a suicide attempt in the past and those who had never made such an attempt (Plutchik et al., 1986). Sensitivity and specificity of the scale are fairly high (Plutchik et al., 1989).
Violence risk. The Past Feelings and Acts of Violence Scale consists of 12 items to be answered on a three-point continuum of frequency. They ask the patient about acts of violence against others, the carrying and use of weapons, arrests, and loss of temper. The internal reliability of the scale is 0.77, indicating high correlations among the items. The scale (in a slightly longer version) has been given to hundreds of individuals from diverse groups: college students, pain patients, epileptics, self-referred violent patients, and prisoners. The results clearly discriminate among most of the groups on average level of expressed violence, with the prisoners and self-referred violent patients scoring highest and the epileptics lowest (Plutchik et al., 1976). In a study of psychiatric inpatients, the scale significantly discriminated between patients reporting violent acts toward others and a group of patients reporting neither suicidal nor violent acts (Plutchik et al., 1986). It has also been used in the study of neuropsychiatric patients and to identify subgroups of violent individuals (Mungas, 1983).

Impulsivity. The Impulsivity Scale consists of 15 items answered on a three-point frequency scale. These items ask about the tendency to engage in impulsive, spur of the moment behaviors, all of which reflect possible loss of control. The scale has an internal reliability of 0.77, indicating a high intercorrelation among items. It has been further described by Plutchik and van Praag (1987).

State and trait anxiety. The Spielberger State-Trait Anxiety Inventory (Spielberger et al., 1970) has been widely used in psychometric research. It consists of two forms—one related to the respondent’s present feelings (state anxiety) and the other related to long-term anxiety (trait anxiety). Both scales have high internal reliability.

Mood. The Mood Adjective Checklist (Plutchik, 1989) measures eight mood constellations, each consisting of a number of related adjectives that are rated on a 0-100 scale by the subject. The mood constellations measured in this study were (1) a composite of emotions related to happiness (interested, sociable, satisfied, and happy), (2) a composite of emotions related to sadness (sad, worried, unhappy, and disappointed), and (3) a composite of emotions related to confusion (confused, indecisive, and surprised).

Anger. The Multidimensional Anger Inventory (Siegal, 1986) was developed for the study of the role of anger in cardiovascular disease after Siegal had found that traditional measures of hostility and aggression did not specifically assess this affect state. The scale measures different dimensions of anger, but in this study we only used the total anger score. This measure has been shown to be reliable, and there is some evidence for good validity. It also correlates with other widely used measures of hostility and aggression (Siegal, 1986). Internal reliability, as measured by coefficient α, is 0.84.

Data Analyses. All test measures were correlated with one another (Pearson product-moment correlation coefficient). The group of 30 patients admitted for attempted suicide was compared on all test measures with the group of nonsuicidal patients by t test. This procedure was repeated in a comparison of the violent group of patients with the nonviolent group.

Results

Table 1 shows the variables that significantly differentiated the patients who had been admitted for a suicide attempt from those who had not. The self-report Suicide Risk Scale score is very significantly higher in the former group, thus providing added external validity for this scale. Of the nine variables used to compare the suicidal and nonsuicidal patients, four are significant. Suicidal patients have higher suicidal risk scores on the self-report scale, have higher violence scores, have higher scores on the trait anxiety measure, and have lower scores on the mood scale measure of happiness. The two groups do not differ significantly on the measures of anger, sadness, state anxiety, impulsivity, and confusion.

Table 2 shows the variables that significantly differentiated between the 40 nonvio-
<table>
<thead>
<tr>
<th>Variable</th>
<th>Suicidal</th>
<th>Nonsuicidal</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suicide risk</td>
<td>13.74</td>
<td>7.00</td>
<td>4.93</td>
<td>0.000</td>
</tr>
<tr>
<td>Happiness</td>
<td>49.29</td>
<td>71.87</td>
<td>-3.41</td>
<td>0.001</td>
</tr>
<tr>
<td>Violence risk</td>
<td>7.93</td>
<td>4.53</td>
<td>2.78</td>
<td>0.01</td>
</tr>
<tr>
<td>Trait anxiety</td>
<td>48.62</td>
<td>40.53</td>
<td>2.47</td>
<td>0.05</td>
</tr>
<tr>
<td>Anger</td>
<td>69.97</td>
<td>59.67</td>
<td>1.74</td>
<td>0.09</td>
</tr>
<tr>
<td>Sadness</td>
<td>57.87</td>
<td>46.63</td>
<td>1.46</td>
<td>0.15</td>
</tr>
<tr>
<td>State anxiety</td>
<td>47.17</td>
<td>41.58</td>
<td>1.46</td>
<td>0.15</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>17.29</td>
<td>14.87</td>
<td>1.35</td>
<td>0.18</td>
</tr>
<tr>
<td>Confusion</td>
<td>40.00</td>
<td>39.33</td>
<td>0.11</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Table 1. Comparison of scores on serotonin-related variables between suicidal and nonsuicidal patients on an acute inpatient unit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonviolent</th>
<th>Violent</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Violence risk</td>
<td>4.63</td>
<td>9.63</td>
<td>-3.92</td>
<td>0.001</td>
</tr>
<tr>
<td>Anger</td>
<td>58.61</td>
<td>77.80</td>
<td>-3.62</td>
<td>0.001</td>
</tr>
<tr>
<td>Suicide risk</td>
<td>8.95</td>
<td>13.45</td>
<td>-2.71</td>
<td>0.01</td>
</tr>
<tr>
<td>Happiness</td>
<td>64.95</td>
<td>51.10</td>
<td>1.97</td>
<td>0.05</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>14.93</td>
<td>18.50</td>
<td>-2.00</td>
<td>0.05</td>
</tr>
<tr>
<td>Trait anxiety</td>
<td>42.71</td>
<td>49.33</td>
<td>-1.75</td>
<td>0.09</td>
</tr>
<tr>
<td>Sadness</td>
<td>48.32</td>
<td>60.60</td>
<td>-1.54</td>
<td>0.13</td>
</tr>
<tr>
<td>State anxiety</td>
<td>45.14</td>
<td>43.67</td>
<td>0.32</td>
<td>0.75</td>
</tr>
<tr>
<td>Confusion</td>
<td>37.51</td>
<td>44.10</td>
<td>-1.00</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Table 2. Comparison of scores on serotonin-related variables between nonviolent and violent patients on an acute inpatient unit

The violent patients had been secluded or restrained because of assault on a staff member or another patient. The Past Feelings and Acts of Violence Scale score for violence risk is significantly higher for the violent than for the nonviolent patients, thus providing further external validity for this scale. Of the nine variables used to compare the violent and nonviolent patients, five are significant. Violent patients have significantly higher violence risk scores on the self-report scale, as well as higher scores on the Multidimensional Anger Inventory, the Suicide Risk Scale, and the Impulsivity Scale. They have lower scores on the "happiness" mood scale. The two groups do not differ significantly on sad moods, state or trait anxiety, or confusion.

Table 3 presents the correlation matrix of the nine variables that were assessed in the study. The suicide risk score correlates significantly with all the other variables, most highly with trait anxiety. Violence risk correlates significantly with all the measures except the three mood scales—happiness, sadness, and confusion.

If we consider the nonsignificant correlations, it appears that sad feelings do not correlate either with violence risk or with impulsivity. Angry feelings do not correlate with state anxiety or with happy feelings. Happy feelings do not correlate with violence.
risk, impulsivity, or anger. Confusion does not correlate with suicide or violence risk, anxiety, or happiness.

Table 3. Correlation between psychometric variables associated with serotonin dysfunction in 60 acute psychiatric inpatients

<table>
<thead>
<tr>
<th>Suicide risk</th>
<th>Violent risk</th>
<th>Impulsivity</th>
<th>State anxiety</th>
<th>Trait anxiety</th>
<th>Happiness</th>
<th>Anger</th>
<th>Sadness</th>
<th>Confusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suicide risk</td>
<td>0.53&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.50&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.47&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.67&lt;sup&gt;1&lt;/sup&gt;</td>
<td>-0.48&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.45&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.48&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.19&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Violent risk</td>
<td>0.39&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.33&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.48&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.03&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.63&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.21&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.15&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Impulsivity</td>
<td>0.33&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.48&lt;sup&gt;1&lt;/sup&gt;</td>
<td>-0.23&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.43&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.16&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.33&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>State anxiety</td>
<td>0.56&lt;sup&gt;1&lt;/sup&gt;</td>
<td>-0.34&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.24&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.31&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.28&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait anxiety</td>
<td>-0.45&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.35&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.49&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.16&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Happiness</td>
<td>0.00&lt;sup&gt;1&lt;/sup&gt;</td>
<td>-0.33&lt;sup&gt;2&lt;/sup&gt;</td>
<td>-0.07&lt;sup&gt;1&lt;/sup&gt;</td>
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<tr>
<td>Anger</td>
<td>0.32&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.40&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>Sadness</td>
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<td></td>
<td></td>
<td>0.36&lt;sup&gt;2&lt;/sup&gt;</td>
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<tr>
<td>Confusion</td>
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1. p < 0.001.<br>2. p < 0.01.

Discussion

The results support the hypothesis that the psychological dimensions that are thought to be related to disturbances of central 5HT metabolism are indeed correlated with one another. This result is not likely to be an artifact of the tests used since there is very little overlap of test items. The Suicide Risk Scale has no common items with the “sadness” mood scale. The Impulsivity Scale has only one item (out of 15) that asks about loss of temper, thus having almost no overlap with the Past Feelings and Acts of Violence Scale or with the Multidimensional Anger Inventory. The Spielberger State-Trait Anxiety Inventory has no items in common with the others. It thus seems reasonable to conclude that the high intercorrelations among the various scales reflect an underlying commonality and are not an artifact of overlapping test items. One hypothesis is that the underlying commonality is the dysregulation of 5HT metabolism.

An alternative hypothesis is that the significant correlations among most of the scales reflect severity of psychopathology. Although this is a possibility, some of the results are inconsistent with it. For example, Table 3 shows that several variables that are not
believed to be related to 5HT metabolism do not correlate well with the others. Neither “happiness” nor “confusion” correlates significantly with violence risk. “Confusion” does not correlate with suicide risk, violence risk, or anxiety. And “happiness” correlates negatively with suicide risk and anxiety.

The considerable reliance in this study on self-report scales merits comment. Although concerns have sometimes been voiced about the possibility of bias or deception, this problem is not limited to self-report tests. Much of the traditional psychiatric interview depends on patient reports, and if bias operates in one context, it operates in the other. More important, perhaps, is the fact that all of the self-report instruments used here have been shown to have high internal reliability and discriminative validity as well. These are important strengths of self-report tests (Plutchik and Conte, 1985), and their presence again suggests that the high intercorrelations among the scales are not an artifact of the methods used.

One of the most interesting findings of this study is the very significant correlation between trait anxiety and suicidal behavior, a relationship that until now has received scant attention in the psychological and biological literature on suicide. The interrelation between anxiety and outwardly directed aggression has also not been extensively researched. On clinical grounds, it seems likely that strong aggressive impulses can either induce or suppress fear. Induction of fear by aggressive impulses is seen in certain phobias (e.g., fear of knives) and obsessions (e.g., fear of killing one’s own children). Psychotherapists have observed that anxiety is often dealt with by aggressive “acting out” in certain individuals (Sandler et al., 1973). As reported here, both Spielberger et al. (1983) and Siegal (1986) have found high correlations between anger and trait anxiety.

The results of the present study support a second hypothesis—that biological indices of brain dysfunction (such as those related to serotonergic transmission) may relate more directly to certain psychopathological dimensions than to diagnostic categories. This hypothesis, put forth by van Praag et al. (1975, 1987, in press) and Brown et al. (1982), could explain the otherwise puzzling finding that a particular biological variable can appear in different diagnostic categories and that the same biological variable can be present in some patients while being absent in others with the same diagnosis. Since the affective dimensions studied here, such as mood lowering, aggression, impulsivity, and anxiety, may vary in idiosyncratic ways in patients regardless of diagnosis, it is at least possible that the precise measurement of these variables in patient populations will help to clarify the reported nonspecificity of 5HT disturbances in psychiatric disorders. Finally, it is obvious that the connections between the various affective dimensions studied here and 5HT disturbances in the brain are hypothetical. Only future research that measures both domains simultaneously will provide more definitive answers.

References


