An 18-Month Followup of Students Biologically at Risk for Psychiatric Problems

by Richard J. Haier, Monte S. Buchsbaum, and Dennis L. Murphy

Abstract

A prospective investigation using platelet monoamine oxidase activity and cortical evoked response augmenting/reducing to predict the onset of new episodes of affective disorders was conducted in a college sample. During an 18-month period between clinical interviews, higher incidences of major depression and hypomania characterized the low MAO/augmenting and the high MAO/reducing subjects. These same subgroups also had been associated with affective psychopathology in the original retrospective study.

Recent investigations suggest that individuals selected from a college population and classified on the basis of high or low platelet monoamine oxidase (MAO) activity and cortical average evoked potential (AEP) augmenting or reducing show a particular pattern of psychiatric problems. In two independent studies (Haier et al. 1980), students with both low MAO and an augmenting evoked potential (LA) and students with high MAO and a reducing evoked potential (HR) showed a higher prevalence of psychopathology than students in the complementary groups with high MAO/augmenting (HA) and low MAO/reducing (LR). According to the Research Diagnostic Criteria (RDC) (Spitzer, Endicott, and Robins 1978), affective disorders most commonly characterized both the LA and the HR students.

This article reports the longitudinal evaluation of one group of students previously classified according to MAO and augmenting/reducing. In addition to the stability of the pattern of psychopathology over time, a primary question investigated is whether the course or severity of the affective disorders initially observed might change in a way that would clarify the specificity between symptoms and biological groups. Also, the issue of vulnerability is addressed directly by determining whether those LA and HR individuals originally not meeting the RDC for any affective disorders subsequently reported episodes of affective disorders.

Method

Subjects. The subjects were identified originally by screening 385 male college student volunteers on the Minnesota Multiphasic Personality Inventory (MMPI). A group of students with highly aberrant MMPI profiles was identified by selecting the 34 of the 385 students who had at least one original MMPI scale T score of 90 or above (over 4 standard deviations above the original population mean on which the MMPI was standardized). A comparison group of 27 students with normal profiles also was selected (see Haier et al. 1980). These 61 subjects completed MAO (Murphy et al. 1976) and evoked potential determinations (Buchsbaum 1974) as well as psychiatric interviews conducted using the Schedule for Affective Disorders and Schizophrenia-life history.
version (SADS-L) (Spitzer and Endicott 1978) and the RDC. The purpose of screening on the MMPI was to identify subjects with serious psychological problems so that the subsequent biological classification could be evaluated with as many different cases as possible. Together, these 61 students represent a group having a very heterogeneous psychological status (ranging from normal with no history of problems to individuals with RDC-defined major depression, bipolar II episodes, antisocial personalities, and serious drug abuse).

Of these 61 subjects, 37 were classified as having either high MAO activity (≥ 11.5 nanomoles/10^8 platelets per hour) or low MAO activity (≤ 8.5). These cutoffs are the upper and lower limits on the high and low MAO groups previously reported (see Haier et al. 1980). Twenty-one of the 37 had aberrant MMPI profiles; 16 had normal profiles. All 37 were classified into augmenting or reducing AEP groups using a median value (1.00 microvolt mv/log foot-lambert) obtained previously (see Haier et al. 1980). Thus, the 37 subjects were categorized into one of four biological groups: low MAO/augmenting (LA, n = 12); low MAO/reducing (LR, n = 11); high MAO/augmenting (HA, n = 5); high MAO/reducing (HR, n = 9). These 37 were the subjects recruited for a followup interview 18 months after the original clinical, psychological, and biological assessments.

Procedure. A research assistant contacted each subject between 17 and 20 months (X = 18) after his initial SADS-L interview and scheduled the followup interview. Because of the practical difficulty of having each subject return to the National Institutes of Health Clinical Center (many had left school and worked full time, others had moved great distances), a telephone interview for everyone was arranged. Also, because affective disorders were most frequently associated with the biological groups, we limited the scope of the telephone interview to inquiries about the presence of new episodes of major depression and hypomania during the interval between the two interviews. The specific SADS-L questions and the RDC for major depression and hypomania were used. The interviewer (who had not participated in the original SADS-L evaluations) did not know either the previous MMPI or RDC status or the biological classification of the subjects. Although not optimal, the telephone and diagnostic scope limitations helped achieve a followup interview rate of 32 out of the 37 possible cases (two declined to be reinterviewed; three could not be contacted).

Results
A new episode of either major depression or hypomania, according to the RDC, occurred during the 18-month interval in 67 percent (14/21) of the combined LA and HR groups. Only 18 percent (2/11) of the combined LR and HA groups reported such episodes during the same 18-month period (Fisher exact test, p < 0.012, 1-tailed). The breakdown by each biological group is: LA—83 percent (10/12); LR—28 percent (2/7); HA—0 (0/4); HR—44 percent (4/9) (see table 1). These results replicate and extend the original study data in which subjects meeting the RDC for any affective disorder (including episodes of major depression, hypomania, minor depression, or depressive personality) were distributed as follows: LA—50 percent (6/12); LR—0 (0/11); HA—20 percent (1/5); HR—55 percent (5/9). Overall, in the original study 52 percent (11/21) of the combined LA and HR groups met the RDC for any affective disorder, whereas only 6 percent (1/16) of the combined LR and HA groups did (p < .005, 1-tailed test) (see Haier et al. 1980).

A more detailed examination reveals a pattern of continuing depressive episodes in the LA and HR groups. All six LA cases originally meeting the RDC for any affective disorder also met the RDC for a new episode of major depression and/or hypomania at followup. Of five HR cases with affective disorders originally, three reported new episodes at followup; the two who did not report new episodes had only met the RDC for minor depression at the original interview. In the LR and HA groups, only one individual originally met the RDC for a minor depression and that case could not be reinterviewed.

We also examined the predictive value of the MAO/AER combinations in individuals who did not report affective episodes at the time of the initial interview. Of the 32 subjects re-interviewed, seven met the RDC for major depression and/or hypomania at followup but had not met the RDC for any affective disorders originally. Were these seven new cases biologically vulnerable? Four (two with major depression, one with hypomania, one with major depression and hypomania) were in the LA; two (one with major depression, one with major depression and hypomania) were in the LR group; and one (with hypomania) was in the HR group. Thus, five of the seven cases were in either the LA or the HR groups. By subgroup, 66 percent (4/6) of the LA group not meeting the RDC for any affective disorders originally did meet the criteria for major
Table 1. Frequency of affective disorders among biological subgroups

<table>
<thead>
<tr>
<th>Biological subgroups</th>
<th>n</th>
<th>Percent at original interview</th>
<th>n</th>
<th>Percent at followup interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low MAO/augmenting</td>
<td>12</td>
<td>50</td>
<td>12</td>
<td>83</td>
</tr>
<tr>
<td>Low MAO/reducing</td>
<td>11</td>
<td>0</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>High MAO/augmenting</td>
<td>5</td>
<td>20</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>High MAO/reducing</td>
<td>9</td>
<td>55</td>
<td>9</td>
<td>44</td>
</tr>
<tr>
<td>Combined LA + HR</td>
<td>21</td>
<td>52</td>
<td>21</td>
<td>67</td>
</tr>
<tr>
<td>LR + HA</td>
<td>16</td>
<td>6</td>
<td>11</td>
<td>18</td>
</tr>
</tbody>
</table>

1. Percent with any affective disorder at original interview.  
2. Percent with major depression and/or hypomania episodes at 18-month followup interview.

depression and/or hypomania at followup. This can be compared with 28 percent (2/7) of LR, 0 (0/4) of HA, and 25 percent (1/4) of HR: these differences, however, do not quite reach statistical significance (note that denominators do not include those subsequently missing from re-interview). Also noteworthy is the fact that three of the four new cases in the LA group originally had normal MMPI profiles as did one of the two new LR cases.

**Comment**

The higher incidence of affective disorder in individuals with either low platelet MAO activity and visual evoked potential augmenting (LA) or high platelet MAO activity and visual evoked potential reducing (HR) that we found in initial interviews (Haier et al. 1980) was maintained 18 months later. New episodes of major depression and hypomania tend to be particularly more frequent among the LA group.

Elsewhere, we have described the sensation-seeking correlates of MAO activity and the sensory inhibition aspect of augmenting/reducing (Haier et al. 1980). Our tentative model of the interaction of these “trait” dimensions describes the LA group as high sensation seekers who lack sensory protection; because of this combination of characteristics, overarousal may result. Overarousal has been hypothesized as a factor in alcoholism, and EP augmenting has been reported in alcoholics (Coger et al. 1976). It is interesting therefore that von Knorring (1976) found that alcoholics were characterized as low MAO augmenters and could be distinguished from other patients with these measures.

The HR group is described as low sensation seeking with sensory inhibition; underarousal may result. So far, specific clinical correlates of this combination have not been identified outside the present sample.

Either combination of LA or HR may produce or affect psychopathological manifestations, but our speculations concerning these variables must be viewed as tentative and treated as hypotheses. Even if the empirical relationships among platelet MAO, augmenting/reducing, and psychiatric problems are substantial, the relationship between possible specific etiology and the biological groupings remains to be investigated. Eventually, the validity of biological classification schemes for psychopathology might best be determined by evaluating the possibility of differential drug responses among biologically defined groups irrespective of the clinical symptoms present (see Buchsbaum and Haier 1978).

As in our previous reports, the level of psychopathology is relatively high for a functioning, college population. This largely results from the MMPI selection criteria for high scores on psychopathology scales. It is also influenced by the use of the Research Diagnostic Criteria which yield high base rates in community surveys (Weissman, Myers, and Harding 1978). These relatively high incidences also occur despite our drawing this sample from a population of community college students living in one of the most affluent and educated counties in the USA. Nonetheless, both prospective and retrospective investigations have demonstrated significant associations between two possibly “high risk” biological variables and affective symptomatology, with similar high incidences of psychiatric symptoms. Additional studies are required in better epidemiological samples and investigating a broader range of psychopathology including alcoholic and schizophrenic symptomatology.

**References**

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