Catecholamine-Thyroid Hormone Interactions: I. Thyroid Hormone and Platelet MAO Activity in Psychiatrically Disturbed Children

by J. Gerald Young, Reza Felz, Jerome A. Roth, Merlyne C. Waldo, and Donald J. Cohen

Abstract

The relation between platelet monoamine oxidase (MAO) activity and serum thyroxine indices was investigated in 68 children and adolescents with a psychiatric disorder and 45 healthy controls. Thyroxine indices were similar in patients and control subjects and neither thyroxine nor estimated free thyroxine levels were significantly related to platelet MAO activity.

Thyroid hormones are intimately related to mood and behavior, as is vividly evident in the anxiety and agitation of hyperthyroidism and the lethargy of the hypothyroid state. Extremes of activity (augmented or reduced) seen in severe developmental disturbances are often target symptoms for medication, and triidothyronine (T3) has been used in the treatment of childhood psychoses with a beneficial effect in some children (Sherwin, Flack, and Stokes 1958; Campbell et al. 1972). The basis for this therapeutic effect is unknown, but the interaction of thyroid hormones with catecholamines or indoleamines might play a role.

Subgroups of autistic children have been characterized by elevated whole blood serotonin (Schain and Freedman 1961) and decreased urinary free catecholamines (Young et al. 1978). Serotonin and the catecholamines are degraded by the intraneuronal enzyme monoamine oxidase (MAO). MAO activity has been reported to have a negative relation with thyroid hormone levels in some animal and human tissues (Skillen, Thienes, and Strain 1961; Levine et al. 1962; Ho-Van-Hap, Babineau, and Berlinguet 1967; Tong and D’Iorio 1976; Feldman and Roche 1977), although not all, and may have a significant regulatory function in nerve endings. In order to clarify whether thyroid function is a source of variance in platelet MAO activity, and to better understand the basis for a therapeutic effect of T3 in some disturbed children, we studied the relation between platelet MAO activity and thyroid indices in children with psychiatric disturbances and a control population.

Population and Method

The subjects of this study were 68 children and adolescents with a psychiatric disorder and 45 healthy controls. The mean age of the 113 subjects was 17.2 years; the patients were younger than the control subjects in both the male (11.9 vs. 27.8 years) and female (12.1 vs. 21.9 years) groups. Each child received a detailed medical and psychiatric evaluation. The severity of disturbance in the patient group ranged from moderate to extreme. All subjects were in good general health at the time of this study.

Twenty-eight percent were taking medication, usually psychotropic drugs, anticonvulsants, or multivitamins. Normal control subjects had no history of medical or psychiatric disturbance either personally or in their families; family control subjects had no medical or psychiatric illness, but were related to a child with a developmental disturbance.

Blood was obtained by standard venipuncture, and collected in...
glass tubes containing 10.5 mg EDTA (K₃) which were immediately placed on ice. Within 3 hours of collection, platelets were separated by centrifugation and stored frozen for a maximum of 14 days before assay. ¹⁴C-Tyramine was used as substrate and platelet MAO activity was expressed as nmoles deaminated product formed per mg protein per 60 minutes of incubation. (Roth, Young, and Cohen 1976).

Thyroxine indices were determined using a competitive protein binding technique (Seligson and Seligson 1972, 1978). Thyroxine (T₄, µg/100 ml) and residual thyroxine binding capacity (TBC, µg/100 ml) were measured and the following derived values were obtained: total thyroxine binding capacity (TTBC, µg/100 ml), percent thyroxine saturation of TTBC (% TS), and estimated free thyroxine (EFT, ng/100 ml).

Results

There were no differences in any of the thyroxine indices among the control and patient groups and all were in the normal range. Male patients had a higher platelet MAO activity than male control subjects, as described elsewhere (Young et al. 1980).

No simple relation emerged when the correlation coefficients for MAO activity and the measured or derived T₄ indices were examined (table 1). There was a trend toward a negative association between MAO activity and thyroxine in the female group, but neither T₄ nor EFT was related to MAO activity in males. There was a significant negative association between MAO and TBC of moderate strength among the females and male controls; this relation did not hold in the overall male population or the male patients. The same relations were examined using third order partial correlations (controlling for age, platelet count, and hematocrit); there was no substantial change from the values given in table 1.

Discussion

Norepinephrine turnover in the rat heart increases following hypophysectomy or thyroidectomy, but returns to normal with thyroid replacement therapy (Landsberg and Axelrod 1968). Plasma norepinephrine (NE) (Christensen 1973; Stoffer et al. 1973), plasma dopamine-β-hydroxylase (DBH) (Noth and Spaulding 1974), and spinal fluid homovanillic acid (HVA) (Klawans and Shenker 1972), the principal brain metabolite of dopamine, are increased in hypothyroidism and decreased in thyrotoxicosis. This negative relation between thyroid state and catecholamine levels has been hypothesized to result from altered β-adrenergic receptor number (Williams et al. 1977; Sterling 1979), or transformation of iodothyronines (tyrosine analogues) into adrenergic neurotransmitters (Dratman 1974; Dratman et al. 1976).

The negative association between thyroid activity and MAO activity in some tissues suggested that MAO might play a part in this regulatory cycle, or might be affected by thyroid function. This would be important to understand for metabolic studies and treatment of severely disturbed children, as well as for elucidating a possible source of variance in studies of platelet MAO activity.

In this study, EFT, the measure of active thyroid hormone in the blood, bore no relation to platelet MAO activity. However, there was

Table 1. Platelet MAO activity and T₄ indices in children with psychiatric disturbances and controls: Pearson correlation coefficients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal controls</th>
<th>Family controls</th>
<th>All controls</th>
<th>Patients</th>
<th>Total population</th>
</tr>
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<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>15</td>
<td>10</td>
<td>25</td>
<td>50</td>
<td>75</td>
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<tr>
<td>MAO—T₄</td>
<td>-.36</td>
<td>-.02</td>
<td>-.18</td>
<td>.12</td>
<td>.08</td>
</tr>
<tr>
<td>MAO—TBC</td>
<td>-.24</td>
<td>-.68**</td>
<td>-.41**</td>
<td>.15</td>
<td>-.02</td>
</tr>
<tr>
<td>MAO—EFT</td>
<td>-.06</td>
<td>.39</td>
<td>.18</td>
<td>.01</td>
<td>.08</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>11</td>
<td>9</td>
<td>20</td>
<td>18</td>
<td>38</td>
</tr>
<tr>
<td>MAO—T₄</td>
<td>-.68**</td>
<td>-.43</td>
<td>-.51**</td>
<td>-.27</td>
<td>-.41*</td>
</tr>
<tr>
<td>MAO—TBC</td>
<td>-.74***</td>
<td>-.72**</td>
<td>-.71****</td>
<td>-.40</td>
<td>-.62***</td>
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<tr>
<td>MAO—EFT</td>
<td>.12</td>
<td>.49</td>
<td>.32</td>
<td>.12</td>
<td>.28*</td>
</tr>
</tbody>
</table>

*p < .10.

**p < .05.

***p < .01.

****p < .001.
a negative association between total T₄ level and MAO activity in females. A moderately strong negative association between residual T₄ binding capacity (TBC) and platelet MAO activity in females and in male controls was notable, but its source and significance are not clear.

This association between platelet MAO activity and residual binding capacity (TBC) in women might reflect a greater total binding capacity (TTBC) secondary to the presence of estrogens and absence of testosterone; TBC tends to parallel MAO activity and residual binding capacity (TBC) in women might reflect a greater total binding capacity (TTBC) secondary to the presence of estrogens and absence of testosterone; TBC tends to parallel MAO activity and residual binding capacity (TBC) in women might reflect a greater total binding capacity (TTBC) secondary to the presence of estrogens and absence of testosterone; TBC tends to parallel TTBC (Robbins, Rall, and Gorden 1974).

The relation between thyroid hormone and platelet MAO activity can be considered from several vantage points. First, there are multiple molecular forms of MAO. The structural basis for these different forms is not yet clear; currently MAO is divided into Type A or Type B according to substrate and inhibitor characteristics (Fowler et al. 1978). The various responses of MAO in different tissues to thyroid hormones may reflect its multiple forms. Second, when T₄ and T₃ are compared, T₃ has been shown to be less firmly bound to protein, to have a shorter biological half-life, and to have a biological activity some four times greater than that of T₄. If T₃ is, in fact, the physiologically active hormone, then it might be useful to measure T₃, rather than T₄. However, most of the T₃ is derived from the peripheral deiodination of T₄, and if the higher concentration of both free and bound T₄ in the plasma is considered together with its longer half-life, the contributions of free T₄ and free T₃ appear to be comparable (Martin 1974; Ingbar and Braverman 1975). Thus, T₄ continues to be the preferred measure for thyroid hormone activity. Third, the age of the organism is crucial when considering the effect of a possible interaction between MAO and thyroid hormones. Thyroid hormones have their major impact on the brain during the critical early period in the life of the young organism. Brain tissue then has mitochondria with a functional site responsive to thyroid hormones, but this sensitivity is lost as the organism matures (Sokoloff 1977). Similarly, the effect of thyroid hormones on heart MAO in male rats changes from an augmenting one in young rats to a diminishing one in the mature animal (Ho-Van-Hap, Barbineau, and Berlinguet 1967). It appears that MAO develops at different rates in different parts of the brain and is subject to a variety of external influences which may alter the course of its development. However, other studies have provided evidence that brain MAO activity in several animals remains remarkably constant with age (Eiduson 1972; Diez and Maderdrut 1977). The subjects in this investigation were much beyond such an early period, and another study of the interaction of platelet MAO activity and thyroid hormone in pregnancy and delivery could clarify these early developmental issues.

References


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