The aromatic amino acids, phenylalanine and tyrosine, are both constituents of protein and tyrosine is the precursor of the catecholamines and thyroid hormone (1). Quantitatively, the amount needed for catecholamine and thyroid hormone synthesis is small (1) and hence dietary requirements are primarily to meet the needs for protein synthesis. Phenylalanine is irreversibly converted to tyrosine in the liver and kidney (2). Provided that there is no limitation in this conversion, dietary aromatic amino acid needs can all be provided as phenylalanine (which we have termed “maximum phenylalanine requirement”). Excess dietary tyrosine will limit the need for dietary phenylalanine to meet the needs for protein synthesis. Therefore, by supplying an excess of tyrosine, it is possible to determine the minimum obligatory phenylalanine requirement (3). The concept of a maximum and minimum phenylalanine requirement is analogous to that of the concept of the maximum and minimum (in the presence of an excess of cysteine) requirements for methionine that we have reported recently (4). In vitro studies in mammalian liver have shown that, in the presence of an excess of exogenous tyrosine, tyrosine derived from phenylalanine hydroxylation is channeled within the hepatocyte directly to oxidation (5).

Determination of amino acid requirements

Amino acid requirements should be determined by feeding graded levels of the test amino acid across a range of intakes, which includes the predicted mean requirement level (6). In the recently published Dietary Reference Intakes (DRI) for the Macronutrients, it was agreed that the isotope oxidation methods are currently the preferred method to determine amino acid requirements (7). Further, it was agreed that the indicator amino acid oxidation (IAAO) model was the best approach. The indicator model is shown in Figure 1. The data used by the DRI committee to define total aromatic amino acid requirements consisted of 3 studies, none of which is ideal. The first used direct amino acid oxidation to determine the minimum phenylalanine requirements in the presence of an excess of tyrosine (40 mg kg\(^{-1}\) d\(^{-1}\)) and studied subjects across a range of 7 levels of phenylalanine intake where each subject was studied at 6 different levels (3). A mean minimum phenylalanine requirement of 9.1 mg kg\(^{-1}\) d\(^{-1}\) was determined with an upper 95% [CI] level of 14 mg kg\(^{-1}\) d\(^{-1}\). A subsequent study using 24-h tyrosine balance as the physiological endpoint and only 3 levels of phenylalanine intake (high, medium, and low) concluded that an intake of 39 mg kg\(^{-1}\) d\(^{-1}\) approximates the daily phenylalanine need (8). The third study was a determination of tyrosine requirements using [\(1^{13}\)]C-lysine as the indicator (9). The subjects of this study ingested a phenylalanine intake of 9 mg kg\(^{-1}\) d\(^{-1}\), which approximates the mean minimum phenylalanine requirement and showed a tyrosine requirement of 6 mg kg\(^{-1}\) d\(^{-1}\) when the phenylalanine intake was at 9 mg kg\(^{-1}\) d\(^{-1}\), for a calculated mean total aromatic amino acid requirement of 15 mg kg\(^{-1}\) d\(^{-1}\). In light of the lack of data, the DRI Committee decided to average the 2 values of 15 and 39 mg kg\(^{-1}\) d\(^{-1}\) and suggested an average total aromatic

Abstract

Dietary aromatic amino acids are needed to meet the requirements for phenylalanine and tyrosine for protein synthesis. The amounts needed for neurotransmitter synthesis and other biological processes are small and quantitatively negligible. The earlier nitrogen balance-based estimates were judged to be inadequate. Very recently, there have been 3 estimates published based on the indicator amino acid oxidation technique, which average 42 mg kg\(^{-1}\) d\(^{-1}\). This average value was obtained by feeding subjects a tyrosine-free diet and hence is an estimate of the mean maximum phenylalanine requirement. The mean minimum phenylalanine requirement estimate in the presence of an excess of tyrosine is 9.1 mg kg\(^{-1}\) d\(^{-1}\). Hence, tyrosine can spare 78% of the dietary phenylalanine need. Finally the optimal proportions of dietary phenylalanine and tyrosine have been shown to be 60:40, respectively. J. Nutr. 137: 1576S–1578S, 2007.
PATTERN OF LABEL OXIDATION IN AN INDICATOR STUDY

FIGURE 1 When the test amino acid intake is limited, all amino acids are in excess and are oxidized to a greater degree. As the intake of the test amino acid increased, then oxidation of the indicator amino acid decreases until the requirement break-point is reached, after which there is a low constant oxidation of the indicator amino acid.

Aromatic amino acid requirement of 27 mg·kg⁻¹·d⁻¹. The only other data in humans using IAAO was in children with phenylketonuria who were shown to have mean tyrosine (10) and phenylalanine (11) requirements of 19 and 14 mg·kg⁻¹·d⁻¹, respectively, for a total mean aromatic amino acid requirement of 33 mg·kg⁻¹·d⁻¹.

Recent estimates of total aromatic amino acid (maximum phenylalanine) requirements

Because it was clear that total aromatic amino acid requirements were not known, we and others have conducted studies in adults in which the only source of aromatic amino acids was phenylalanine. In the first study, we used [1-¹³C]-lysine as the indicator and derived a mean requirement of 48 mg·kg⁻¹·d⁻¹ (12). Next, we attempted to utilize [1-¹³C]-leucine as an indicator amino acid to determine aromatic amino acids. Despite leucine being used as an indicator amino acid, its use, to our knowledge, had never been validated (6). We found that leucine is not a good indicator and that it was important to use a limited intake of leucine in order for the indicator to have any sensitivity (13). The derived mean estimate of total aromatic amino acid requirements was 42 mg·kg⁻¹·d⁻¹. Most recently, Kurpad et al. (14) have reported the use of 24-h indicator oxidation and balance using [¹³C]-leucine to determine total aromatic amino acid needs. Their estimate of the maximum phenylalanine requirement is 38 mg·kg⁻¹·d⁻¹. The main criticism of the Kurpad et al. (14) article is that their range of intakes is narrow and ranges from 19 to 47 mg·kg⁻¹·d⁻¹. In our work, we used phenylalanine intake ranging from 5 to 70 mg·kg⁻¹·d⁻¹. Because of the narrow upper end of their range, the Kurpad et al. (14) studies have only 2 data points above the requirement break-point. We in fact had a similar problem with our lysine indicator studies and had to add additional phenylalanine intake levels to define the requirement break-point with certainty. Had Kurpad et al. (14) used additional levels of phenylalanine intake above the break-point, we suggest that their break-point requirement value would have been higher and would have been similar to our own.

Aromatic amino acid requirement estimates are summarized in Table 1 and included for historical purposes are the 1985 FAO/WHO/UNU estimates based on nitrogen balance (15).

The sparing of phenylalanine by tyrosine

As mentioned above, the minimum phenylalanine requirement has been defined as being 9.1 mg·kg⁻¹·d⁻¹ (3). From the 3 studies of the maximum phenylalanine requirement that range from 38 to 48 mg·kg⁻¹·d⁻¹, the proportion of the total aromatic amino acid requirement that can be met by tyrosine ranges between 76 and 81%. The study of Roberts et al. (9) casts a different light on the relation between phenylalanine and tyrosine. At a phenylalanine intake limited to 9 mg·kg⁻¹·d⁻¹, protein synthesis was optimized at a mean tyrosine intake of 6 mg·kg⁻¹·d⁻¹. This suggests that for optimal protein synthesis, the optimal dietary ratio of phenylalanine and tyrosine in mass units is 60:40. This ratio is similar to that seen in human tissue (7,16). Three recent studies have established clearly that the requirement for phenylalanine (to meet the needs for phenylalanine plus tyrosine) is an average of 43 mg·kg⁻¹·d⁻¹. The optimal dietary ratio of phenylalanine to tyrosine is 60:40.

TABLE 1 Summary of aromatic amino acid requirements for healthy adults

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Method Used</th>
<th>Test Amino Acids</th>
<th>EAR</th>
<th>RDA</th>
</tr>
</thead>
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<tr>
<td>FAO/WHO (15)</td>
<td>N Balance</td>
<td>Phe + Tyr</td>
<td>14</td>
<td></td>
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<tr>
<td>Zello (3)</td>
<td>IAAO</td>
<td>Phe (plus excess Tyr) 9.1</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Basile-Filho (8)</td>
<td>24-h Tyr balance</td>
<td>Phe + Tyr</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Roberts (9)</td>
<td>IAAO</td>
<td>Tyr</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Hsu (12)</td>
<td>IAAO</td>
<td>Phe</td>
<td>44–52</td>
<td></td>
</tr>
<tr>
<td>Hsu (13)</td>
<td>IAAO</td>
<td>Phe</td>
<td>42</td>
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</tr>
<tr>
<td>Kurpad (14)</td>
<td>24-h IAAO/balance</td>
<td>Phe</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

EAR, Estimated average requirement; RDA, recommended daily allowance; IAAO, direct amino acid oxidation; IAAO; Phe, phenylalanine; Tyr, tyrosine.

Literature Cited

4. Ball RO, Courtney-Martín G, Pencharz PB. The in vivo sparing effect of tyrosine plus tyrosine) is an average of 43 mg·kg⁻¹·d⁻¹. The optimal dietary ratio of phenylalanine to tyrosine is 60:40.


