The impact of dietary amino acids on the mental health of older overweight adults

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Abstract

Background
The aim of this study was to examine the relationship between dietary amino acids and mental health for overweight and obese older (55+) adults.

Methods
168 overweight, older (mean age 62.7 ± 5.5) adults (n=65 men, n=103 women), completed the RAND-36 item Health Survey (RAND-36) and kept a 3-day food record in this cross-sectional study. The relationship between the dietary amino acid intake as percentage of protein and the MCS (Mental Component Score) was assessed using linear regression analysis. The model was verified for the following covariates: sex, age, body mass index (kg/m²), PCS (Physical Component Score) and total energy intake per day (kilocalories).

Results
Intake of all amino acids and groups of amino acids was strongly and significantly correlated (Pearson correlation coefficients: 0.81-0.99). Mean MCS was 11% lower in case of a deficiency, though this difference was not significant. Relationships were found for isoleucine (β=8.467, p=0.000), leucine (β=4.677, p=0.000), methionine (β=10.026, p=0.012), phenylalanine (β=7.840, p=0.001), tyrosine (β=8.613, p=0.001), threonine (β=7.137, p=0.006), tryptophan (β=29.979, p=0.001), valine (β=5.395, p=0.003), glutamic acid (β=0.930, p=0.019), proline (β=1.983, p=0.021), serine (β=6.543, p=0.001), branched-chain amino acids (BCAA’s, β=2.026, p=0.001), aromatic amino acids (AR’s, β=3.980, p=0.001) and large neutral amino acids (LNAA’s, β=1.370, p=0.001) expressed as a percentage of protein intake. The AR versus BCAA intake was negatively related (β=−86.808, p=0.036) with the MCS.

Conclusion
Dietary amino acids and groups of dietary amino acids, expressed as a percentage of total protein intake, show significant relationships with mental health for older, overweight adults.

Key words
Amino acids, mental health, overweight, older adults, nutrition.
The impact of dietary essential amino acids on the mental health of older overweight adults
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The impact of dietary essential amino acids on the mental health of older overweight adults
Introduction

The World Health Organization (WHO) recently stated that mental health problems are the main cause of disability and early retirement as well as a major burden to the economy in the European Union (1). Total costs due to poor mental health in Europe are estimated to be 3-4% of gross national product (GDP), around 500 billion euro in 2014 (2).

Mental health is defined as a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community (3). Mental health is an integral and essential component of health (1) and it is negatively influenced by a sedentary lifestyle, a poor diet, short sleep, substance misuse and psychosocial factors (e.g. competition, time pressure and social isolation) (4).

Recently several studies have been published on the relationship between diet and mental health. A large Australian cohort study concluded that older adults with high quality diets (e.g. Mediterranean diet) report a better health-related quality of life. Men showed a significant association between a dietary guideline index (DGI) and an overall mental component summary scale (OR=1.51, 95% CI: 1.07-2.15), while the DGI for women was associated with emotional wellbeing (OR=1.53, 95% CI: 1.11-2.10) (5). Cross-sectional and longitudinal studies show a relationship between dietary quality, depressed mood and anxiety. An increased risk of depression was observed in a cohort study of middle-aged office workers in Britain (n=3,486) eating a Western style diet, while office workers eating a whole foods diet showed a lower risk (4). A large European study (n=10,094 middle-aged professionals) found that the more people adhere to a Mediterranean diet, the lower the risk for depression over a period of approximately four years (with the group that adhered most to the Mediterranean diet of a total of 5 groups, showing a 0.58 hazard ratio (95% CI: 0.44-0.77) compared to 1 for the control group with lowest adherence) (6). Other research shows that the traditional Japanese as well as the Mediterranean diet, vegetarian diets and diets with relatively more fish (omega 3 fatty acids), vegetables and cereals, significantly decrease the odds of depression (7-11). A systematic review of 21 observational studies on two dietary patterns (healthy diet and Western diet) summarizes that high intakes of fruit, vegetables, fish and whole grains (healthy diet) are significantly associated with a reduced risk of depression (OR=0.84, 95% CI: 0.76-0.92, p<0.001, based on 13 studies) (7).

Conversely the same applies to unhealthy diets. A high intake of sweets, fast food and processed pastries is related to an increased risk of depression (11). Research also suggests that the relation is not reversible: depression does not seem to cause poor dietary choices (6). Better psychological well-being is also not due to weight loss as a result of a healthier diet, which could have been the case since obesity and anxiety seem to have a positive relation (12). There is however no strong evidence that losing weight itself results in less anxiety, although none of the assessed studies shows an increase in anxiety as a result of intended weight loss (12).

Mechanisms of the impact of nutrition on mental health are still not fully understood, although it is clear that inflammation plays an important role (11,13). Micronutrients mentioned as essential for neurochemical functioning are B vitamins, zinc, magnesium, vitamin C and a range of plant compounds like flavonoids (anti-oxidant and anti-inflammatory) (4,13,14) and more recently also vitamin D (15).
Macronutrients are also related to mental health. Carbohydrates are associated with an increased uptake in the brain of tryptophan, an essential amino acid and precursor of the neurotransmitter serotonin (11). Essential fatty acids and more specific eicosapentaenoic acid (EPA) seem essential macronutrients for the brain and research shows that EPA and docosahexaenoic acid (DHA) benefit people with mental health challenges (4,13-16).

Research on dietary protein and mental health is limited, but it seems that high protein food can increase alertness (14). Individual dietary amino acids on the other hand, are mentioned more often as essential compounds for mental health (4).

Tryptophan, an essential amino acid and precursor of serotonin, has been used to increase brain levels of serotonin since the 1970’s. Tryptophan alone however seems insufficient to boost serotonin. Transport of tryptophan into the brain is related to the total amount of large neutral amino acids (LNAA’s: tryptophan, phenylalanine, tyrosine, leucine, isoleucine and valine). A higher tryptophan-LNAA ratio seems to cause increased serotonin levels (17). But also the ratio tryptophan-BCAA’s ( Branched-Chain Amino Acids: isoleucine, leucine and valine) appears to be able to increase the tryptophan available to the brain (18). The AR’s (Aromatic amino acids: phenylalanine, tyrosine, tryptophan and histidine) and in particular tyrosine are linked to the synthesis of serotonin, dopamine, noradrenalin and adrenalin. Ingesting high amounts of BCAA’s however, seems to lower concentrations of AR’s and hence the production of serotonin and the catecholamines (19,20). An animal study shows that low levels of isoleucine alone are also related to depression (21).

While emerging data provide insights and may give rise to future research, evidence for causality between diet and depression is still minimal (4) and pathways remain unclear. Pathways for dietary amino acids and their influence on mental health on the other hand are described more often, but are less supported with human studies (17,19-22).

One Malaysian study (n=30) suggests that addition of tryptophan-rich talbinah (a local dish) to the diet can cause a significant reduction of depression and increase of mood in depressed, institutionalized older (60+) adults. Scores on the Geriatric Depression Scale (GDS-R) decreased from 6.6 (± 3.1) to 3.7 (± 2.7) with p<0.05 in this 7-week trial (18). Other research shows that tryptophan and phenylalanine supplementation enhances the effectiveness of antidepressants (23). A double blind randomized controlled trial performed in Syria shows that lysine fortification can reduce anxiety and stress in family members in economically weak communities (24). One Finish study however, examined the relation between dietary intake of amino acids and low mood, but did not find any association (25).

Overall, the body of evidence for an association between amino acids and mental health is inconsistent and asks for more human studies.

Objective
The aim of this cross-sectional study is to examine the relationship between dietary amino acids and mental health.
Methods

A cross-sectional study of baseline data collected from two randomized controlled trials on protein-enriched diets with exercise programs for overweight 55+-aged community dwelling Dutch men and women was performed. Subjects were eligible when physically fit and as long as they had not participated in a weight loss program 3 months before baseline assessment. The studies were not specifically designed to assess the relationship between amino acid intake and mental health. Intake was measured as general independent variable and mental health was assessed as a secondary outcome.

Subjects

Baseline data of two studies were used. In both studies general information was collected during the first visit: weight and length were respectively measured on a calibrated scale and a wall-mounted stadiometer.

The 13-week Muscle Preservation Study (MPS) conducted in 2011-2012, examined the effect of a whey protein-, leucine- and vitamin D-enriched supplement on 80 obese (BMI [in kg/m2] ≥30 or BMI ≥28 with waist circumference >102 cm for men and >88 cm for women) 55+-aged adults. Forty participants were randomly assigned to the supplement and 40 to an isocaloric control product. All subjects participated in a 3-hour per week resistance exercise and hypocaloric (600 kilocalories below estimated energy needs) diet program. Verreijen et al (26) gave an extensive explanation of used methods in the MPS.

The 10-week Weight Loss with Protein and Resistance Exercise in Overweight Older Adults (WelPrex) study, examined the effect of diet and exercise by following 100 subjects, randomized into 4 groups:

1. Control group (n=22), regular diet (0.8 g protein/kg body weight) and exercise advice (following general Dutch guidelines);
2. High protein diet group (n=21): high protein diet (1.3 g protein/kg body weight) and exercise advice (following general Dutch guidelines);
3. Exercise group (n=25): regular diet and resistance exercise program;
4. High protein and exercise group (n=32): high protein diet and resistance exercise program.

A description of the two studies is available online in the Dutch Trial register (27,28).

Assessment of amino acid intake

In both studies food-intake was assessed at baseline, halfway and at completion. A 3-day food-record was used before each assessment and was checked and verified for completeness and correctness during visits. Energy and macronutrient intake were calculated using the Dutch Food Composition Table (29). We retrieved additional data on the amino acid composition of food from the British McCance and Widdowson’s by Paul et al (30).

Intake of the (semi-)essential amino acids was compared with amino acid requirements as defined by the World Health Organization to establish potential deficiencies (31).

Assessment of mental health

In both studies the RAND-36 item Health Survey (RAND-36) was used to assess the general health status of participants at baseline, halfway and at completion. The RAND-36 is based on the three pillars of the World Health Organization’s (WHO) definition of health: physical, mental and social well-being (32). The RAND-36 has scales for physical functioning, social functioning, role limitations caused by physical health problems, role limitations caused by emotional
problems, emotional well-being, energy/fatigue, pain and general health perceptions (32). The RAND-36 also has a physical component score (PCS) and a mental component score (MCS). General health perceptions, energy/fatigue and social functioning are included in both scores, whereas role limitations caused by emotional problems and emotional wellbeing are exclusive for mental health (33).

Statistical analysis
Baseline characteristics of the study population were assessed using independent t-tests. The relationship between the dietary amino acid intake and mental health was examined using linear regression analysis. Amino acid intake was expressed as percentage of total protein intake and related to the dependent variable MCS. The model was verified for the following possible covariates: sex, age, body mass index in kg/m², PCS and total mean energy intake per day at baseline in kilocalories. Statistical significance was defined as p < 0.05.

All statistical tests were performed using IBM SPSS Statistics version 22.
Results

Subject characteristics
The number of screened subjects, inclusion, exclusion and baseline totals are presented in the flowchart (figure 1). MCS and amino acid intake were calculated for 168 participants. The baseline characteristics are summarized in table 1. The difference in age between men and women was significant with men being on average 2 years older. Mean body mass index in kg/m² was 1.4 lower for subjects who participated in the WelPrex, they consumed more protein and showed a slightly different intake of leucine, tyrosine and AR’s (in protein percentages) then subjects in the MPS. For the other baseline characteristics no significant differences were found (see table 1).

Relationship between amino acid intake and mental health
Intake of isoleucine, leucine, methionine, phenylalanine, tyrosine, threonine, tryptophan, valine, glutamic acid, proline and serine –expressed as percentage of total protein intake– resulted in a significant increase of the MCS. Significant relationships were also found for the BCAA’s, LNAA’s, AR’s and the MCS. The essential amino acids lysine, histidine, the semi-essential cysteine, the non-essential amino acids alanine, aspartic acid and glycine were not significantly related to the MCS. Also plant- and animal based protein (as percentage of total protein) showed no relationship with mental health. Relative intake of tryptophan to LNAA-group, tryptophan to BCAA-group and AR-group to BCAA-group were also examined. These relationships turned out to be negative and not significant, except for the AR/BCAA relation (β=-86.808, p=0.036). Table 2 shows regression coefficients and significance for all studied amino acids, the amino acids groups and the MCS. Significant relationships are graphically illustrated and presented in appendix 2.

None of the covariates (sex, age, body mass index in kg/m², PCS and total mean energy intake per day at baseline in kilocalories) showed to be confounding for the significant relations.

Absolute intake of all amino acids and groups of amino acids are strongly and significantly correlated with Pearson correlation coefficients ranging from 0.81 to 0.99. Mean MCS was on average 11% higher (not significant), for non-deficient subjects compared to MCS’s for subjects with an amino acid deficiency (specified in table 3).
**Figure 1:** Flowchart of baseline totals of MPS and WelPrex trials.
Table 1: Baseline characteristics (with amino acids as percentage of total protein intake) of all the subjects from the MPS versus the WelPrex study.

<table>
<thead>
<tr>
<th></th>
<th>All subjects (n=168)</th>
<th>MPS (n=77)</th>
<th>WelPrex (n=91)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>AGE</td>
<td>62.7</td>
<td>5.5</td>
<td>62.9</td>
<td>5.4</td>
</tr>
<tr>
<td>BMI kg/m2</td>
<td>32.7</td>
<td>4.4</td>
<td>33.3</td>
<td>4.5</td>
</tr>
<tr>
<td>MCS</td>
<td>50.5</td>
<td>10.5</td>
<td>49.8</td>
<td>9.5</td>
</tr>
<tr>
<td>PCS</td>
<td>48.8</td>
<td>7.8</td>
<td>48.7</td>
<td>8.9</td>
</tr>
<tr>
<td>Energy intake (kcal)</td>
<td>1928.4</td>
<td>610.1</td>
<td>1890.6</td>
<td>585.7</td>
</tr>
<tr>
<td>Protein intake (g)</td>
<td>83.3</td>
<td>25.8</td>
<td>79.0</td>
<td>23.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>As % of protein:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoleucine</td>
<td>4.5</td>
<td>0.3</td>
<td>4.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Leucine</td>
<td>7.8</td>
<td>0.6</td>
<td>7.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Lysine</td>
<td>6.4</td>
<td>0.8</td>
<td>6.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Methionine</td>
<td>2.2</td>
<td>0.2</td>
<td>2.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Cysteine</td>
<td>1.5</td>
<td>0.2</td>
<td>1.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>4.6</td>
<td>0.3</td>
<td>4.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>3.4</td>
<td>0.3</td>
<td>3.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Threonine</td>
<td>3.9</td>
<td>0.3</td>
<td>3.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>1.2</td>
<td>0.1</td>
<td>1.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Valine</td>
<td>5.4</td>
<td>0.4</td>
<td>5.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Arginine</td>
<td>5.2</td>
<td>0.5</td>
<td>5.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Histidine</td>
<td>2.7</td>
<td>0.3</td>
<td>2.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Alanine</td>
<td>4.5</td>
<td>0.5</td>
<td>4.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>8.2</td>
<td>0.7</td>
<td>8.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>19.8</td>
<td>2.0</td>
<td>19.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Glycine</td>
<td>3.9</td>
<td>0.5</td>
<td>3.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Proline</td>
<td>7.0</td>
<td>0.9</td>
<td>7.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Serine</td>
<td>4.9</td>
<td>0.4</td>
<td>4.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Plant protein</td>
<td>38.4</td>
<td>11.6</td>
<td>38.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Animal protein</td>
<td>61.6</td>
<td>11.6</td>
<td>61.6</td>
<td>0.1</td>
</tr>
<tr>
<td>BCAA</td>
<td>10.0</td>
<td>8.8</td>
<td>17.5</td>
<td>1.7</td>
</tr>
<tr>
<td>AR</td>
<td>9.2</td>
<td>0.7</td>
<td>9.1</td>
<td>0.6</td>
</tr>
<tr>
<td>LNAA</td>
<td>19.2</td>
<td>9.0</td>
<td>26.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>
**Table 2:** MCS for subjects with and without an (semi-)essential amino acid deficiency, based on WHO amino acid requirements (31).

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Subjects with deficiency</th>
<th>Mean MCS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percentage</td>
<td>Deficient</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>7</td>
<td>4.2%</td>
<td>43.9</td>
</tr>
<tr>
<td>Leucine</td>
<td>9</td>
<td>5.4%</td>
<td>47.2</td>
</tr>
<tr>
<td>Lysine</td>
<td>10</td>
<td>6.0%</td>
<td>48.0</td>
</tr>
<tr>
<td>Methionine</td>
<td>8</td>
<td>4.8%</td>
<td>45.5</td>
</tr>
<tr>
<td>Cysteine</td>
<td>1</td>
<td>0.6%</td>
<td>41.8</td>
</tr>
<tr>
<td>Phenylalanine (with tyrosine)</td>
<td>2</td>
<td>1.2%</td>
<td>48.4</td>
</tr>
<tr>
<td>Threonine</td>
<td>5</td>
<td>3.0%</td>
<td>45.7</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>3</td>
<td>1.8%</td>
<td>45.2</td>
</tr>
<tr>
<td>Valine</td>
<td>9</td>
<td>5.4%</td>
<td>47.5</td>
</tr>
<tr>
<td>Histidine</td>
<td>5</td>
<td>3.0%</td>
<td>45.7</td>
</tr>
</tbody>
</table>

*Intake and requirement of amino acids is compared based on daily intake in mg per kg body weight.*
Table 3: Regression coefficients $\beta$ and $p$-values for the relationships between intake of (groups of) amino acids and dependent variable MCS.

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>$\beta$</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoleucine</td>
<td>8.467</td>
<td>0.000</td>
</tr>
<tr>
<td>Leucine</td>
<td>4.677</td>
<td>0.000</td>
</tr>
<tr>
<td>Lysine</td>
<td>1.281</td>
<td>0.224</td>
</tr>
<tr>
<td>Methionine</td>
<td>10.026</td>
<td>0.012</td>
</tr>
<tr>
<td>Cysteine</td>
<td>7.654</td>
<td>0.129</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>7.840</td>
<td>0.001</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>8.613</td>
<td>0.004</td>
</tr>
<tr>
<td>Threonine</td>
<td>7.137</td>
<td>0.006</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>29.979</td>
<td>0.001</td>
</tr>
<tr>
<td>Valine</td>
<td>5.395</td>
<td>0.003</td>
</tr>
<tr>
<td>Arginine</td>
<td>1.589</td>
<td>0.281</td>
</tr>
<tr>
<td>Histidine</td>
<td>4.634</td>
<td>0.138</td>
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<tr>
<td>Alanine</td>
<td>2.350</td>
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<td>1.162</td>
<td>0.292</td>
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<td>Glutamic acid</td>
<td>0.930</td>
<td>0.019</td>
</tr>
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<td>Glycine</td>
<td>0.977</td>
<td>0.534</td>
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<td>Proline</td>
<td>1.983</td>
<td>0.021</td>
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<tr>
<td>Serine</td>
<td>6.543</td>
<td>0.001</td>
</tr>
<tr>
<td>BCAA</td>
<td>2.026</td>
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<tr>
<td>AR</td>
<td>3.980</td>
<td>0.001</td>
</tr>
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<td>LNAA</td>
<td>1.370</td>
<td>0.001</td>
</tr>
<tr>
<td>Plant protein</td>
<td>-0.031</td>
<td>0.658</td>
</tr>
<tr>
<td>Animal protein</td>
<td>0.031</td>
<td>0.658</td>
</tr>
<tr>
<td>TRP/LNAA</td>
<td>-217.551</td>
<td>0.688</td>
</tr>
<tr>
<td>TRP/BCAA</td>
<td>-221.823</td>
<td>0.478</td>
</tr>
<tr>
<td>AR/BCAA</td>
<td>-86.808</td>
<td>0.036</td>
</tr>
</tbody>
</table>

$\beta$-regression coefficient, amino acids, BCAA, AR, LNAA, plant protein and animal protein are expressed as percentage of total protein. TRP/LNAA, TRP/BCAA and AR/BCAA are relative totals in mg.
The impact of dietary essential amino acids on the mental health of older overweight adults
Discussion

This study shows that intake—expressed as percentage of protein—of isoleucine, leucine, methionine, phenylalanine, tyrosine, threonine, tryptophan, valine, glutamic acid, proline, serine, BCAA’s (isoleucine, leucine and valine), AR’s (phenylalanine, tyrosine and tryptophan) and LNAA’s (sum of BCAA’s and AR’s), is significantly and positively related to mental health. It also shows that a deficiency in all (semi-)essential amino acids can be related to a lower MCS, although this effect is not significant.

The mean MCS for the studied subjects was 50. Research has found that the MCS-values below 42-45 can be good predictors of depressive disorders based on DSM-III-R criteria with a sensitivity of 71% and a specificity of 82% (34). MCS’s below this range were found in the present study for subjects with a deficiency in isoleucine and cysteine.

The results for the AR’s (phenylalanine, tyrosine and tryptophan) were expected, based on previous research (11,17-20,23,35), as were results for isoleucine (11,21) and valine (11). Since the latter two are BCAA’s, a relation between mental health and the BCAA’s as a group was foreseen as well and the same rational can be applied to the LNAA’s (sum of BCAA’s and AR’s).

Although Smriga et al (24) found a relationship between lysine, anxiety and stress, which could indicate some influence of lysine on mental health, this relationship was not confirmed by the findings of this study. This could be explained by the fact that Smriga et al examined the effect on people suffering from depression, whereas the MPS and the WelPrex study did not included people with mental diseases.

Relationships between mental health and leucine, methionine, threonine, glutamic acid and serine are rather surprising, although methionine, glutamic acid and serine have been mentioned as enhancers of the production of glutathione, an anti-oxidant that has been linked in theories on the effect of oxidation in the brain (13).

The present study shows that tryptophan has an impact on mental health. The impressive effects of tryptophan depletion are studied mostly in depressed patients. Research shows for example that a protein mixture containing amino acids without tryptophan can cause a 42% decrease of human plasma tryptophan and an 85% decrease in serotonin (35). Other research shows reversal of depression after intravenous tryptophan (23), although later research concludes that the effects of tryptophan supplementation are questionable (25). Effects of serotonin manipulation in healthy adults under normal conditions seem to be small or negligible (35) and are only identified in case of stressful situations (17). This cross sectional study however shows that tryptophan is also related to mental health for healthy, overweight older adults in a not specifically stressful situation. Tryptophan however can only be converted into serotonin when other nutrients are available as well. It needs carbohydrates, omega-3 fatty acids EPA and DHA, (preferably combined with vitamin D), vitamin B6 and magnesium (17,18,23). Therefore it is premature to confirm the relation tryptophan-mental health for healthy subjects.

The findings of the present study are in contrast with a Finish cohort study, which concluded that there is no relationship between amino acid intake and low mood among 50-69 year old adults (25). Some important differences however may explain the differences in outcome. The Finish cohort consisted of male only smokers instead of a diverse group of older men and women. Diet was assessed using a dietary history method, based on the frequency of
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consumption of specified food items, which gives an indication, but is not perceived to be as accurate and precise as the 3-day food record (comparable with the 24-hour recall method) used for the MPS and WelPrex study (36). And finally the study defined low mood as either self-reported depressed mood, hospital admission due to major depressive disorder and suicide, whereas the RAND-36 MCS defines mental health on a continuum (33).

More insight -especially on the effects of amino acid deficiency- could have been achieved with more subjects. The study also lacked more detailed insight on subjects’ current and previous suffering of depression and use of anti-depressants, due to the fact that the data were collected for other research-objectives.

The complex pathways of amino acids, neurotransmitters and catecholamine’s, underline the fact that it is very difficult to assess the impact of individual nutrients on mental health. The strong correlation between the amino acids gives an impression of all the possible links and synergies between many different nutrients.

We see that traditional diets rich in fruit and vegetables (e.g. the Mediterranean diet) are positively related to mental health (4,7,11,37), but that eating more fruit and vegetables alone does not seem to give such clear results (38). Food patterns often create a still not well-understood synergy (39).

For practical use it is of course more relevant to understand which diet or food pattern leads to better health. On the other hand, we need single nutrient research (preferably randomized controlled trials) to elucidate the pathways. The research on the relationship between food and mental health is too overwhelming and too promising to leave it to a general dietary prescription without knowing the mechanisms. This however should not stop us from introducing dietary recommendations in the treatment of people with poor mental health and prevention, based on research outcomes that are already available. This is relevant, since medication seems to have a negligible impact on people with mild to severe depression (40). The International Society for Nutritional Psychiatry Research (ISNPR) argued recently that diet and nutrition should be integrated in the standard practice of psychiatry, both as cure but also as prevention (41). Members of the ISNPR also call for trial designs to explore individualized tailored programs to research the effect of ‘lifestyle medicine’ on depression (4).

Future research should shed light on the relationships between specific (groups of) amino acids and mental health and the effects of supplementation on both healthy subjects as well as patients. On a practical level, physicians working with mentally diseased patients and dieticians should join forces, both in research as in practice, to improve the lifestyle of people suffering from poor mental health.
Conclusion

Dietary amino acids and groups of dietary amino acids, expressed as a percentage of total protein intake, show significant relationships with mental health for older, overweight adults.
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References


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Appendix 1: abbreviations

AR  Aromatic amino acids (phenylalanine, tyrosine, tryptophan and histidine)
BCAA  Branched-chain amino acids (isoleucine, leucine and valine)
CI  Confidence interval
DGI  Dietary guideline index
DHA  Docosahexaenoic acid (long chain omega-3 fatty acid)
EPA  Eicosapentaenoic acid (long chain omega-3 fatty acid)
GDS-R  Geriatric Depression Scale
LNAA  Long neutral amino acids (isoleucine, leucine, valine, phenylalanine, tyrosine, tryptophan and histidine)
MCS  Mental Component Score
MPS  Muscle preservation study
OR  Odds ratio
PCS  Physical Component Score
WHO  World Health Organization
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Appendix 2: graphical presentation relationships amino acids and MCS

**Figure 2**: Relation isoleucine (% protein) and MCS:
MCS = 12.3 + (8.5 x isoleucine % protein)

**Figure 3**: Relation leucine (% protein)-MCS:
MCS = 14.1 + (4.7 x leucine % protein)

**Figure 4**: Relation methionine (% protein) and MCS:
MCS = 28.3 + (10.0 x methionine % protein)

**Figure 5**: Relation phenylalanine (% protein) and MCS:
MCS = 14.8 + (7.8 x phenylalanine % protein)

**Figure 6**: Relation tyrosine (% protein) and MCS:
MCS = 20.9 + (8.6 x tyrosine % protein)

**Figure 7**: Relation threonine (% protein) and MCS:
MCS = 22.5 + (7.1 x threonine % protein)
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Figure 8: Relation tryptophan (% protein) and MCS: 
MCS = 14.2 + (30.0 x tryptophan % protein)

Figure 9: Relation valine (% protein) and MCS: 
MCS = 21.7 + (5.4 x valine % protein)

Figure 10: Relation glutamic acid (% protein) and MCS: 
MCS = 32.2 + (0.9 x glutamic acid % protein)

Figure 11: Relation proline (% protein) and MCS: 
MCS = 36.7 + (2.0 x proline % protein)

Figure 12: Relation serine (% protein) and MCS: 
MCS = 18.3 + (6.5 x serine % protein)

Figure 13: Relation BCAA’s (% protein) and MCS: 
MCS = 14.8 + (2.0 x BCAA % protein)
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**Figure 14:** Relation AR’s (% protein) and MCS: 
MCS = 13.9 + (4.0 x AR % protein)

**Figure 15:** Relation LNAA’s (% protein) and MCS: 
MCS = 13.7 + (1.4 x LNAA % protein)

**Figure 16:** Relation AR/BCAA and MCS 
MCS = 109.4 - (86.8 x AR/BCAA in mg)