

Characterization of a metabolomics signature of the brain-health-promoting MIND diet in older persons

P2-13

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We identified a blood metabolomics signature of the MIND diet in older adults composed of 8 food-related metabolites. The increase of this metabolomic signature was associated with 37% lower odds of accelerated cognitive decline over 12 years.

| INTRODUCTION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | METHODS                                                                                                                                                                                                                                                                                                               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| <p>The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) is associated with reduced cognitive decline (1).</p> <p>→ The underlying biological pathways remain unclear. Developing a panel of objective biomarkers for adherence to this diet could give novel insights on such mechanisms and might help to identify target populations for clinical trials or prevention programs aimed at lowering cognitive aging through nutritional strategies.</p> <p>The objective of this study was to characterize a blood metabolomic signature of adherence to the MIND diet and evaluate its prospective association with cognitive trajectories in older adults from the general population.</p> | <p>Case-control sample nested in the 3C cohort study (65y+, non-institutionalized) (2)</p> <div><div><div>1999+2y+4y+7y+10y+12y</div><div>Cognitive tests → cognitive decline case-control (accelerated or not)</div></div><div><div>Targeted metabolomics UHPLC MS/MS 155 metabolites</div><div>Dietary survey (FFQ, R24) MIND adherence score</div></div><div><div>STEP 1</div><div>Identification of a metabolomic signature of adherence to the MIND Diet (N=344, Bootstrap-enhanced LASSO penalized regression)</div></div><div><div>STEP 2</div><div>a) Construction of the « MIND metaboscore » (∑ concentrations of identified metabolites weighted by their association with MIND adherence)</div><div>b) Estimation of its association with cognitive decline status (N=418 &amp; N=420, conditional logistic regressions)</div></div></div> <p>French-adapted MIND diet adherence (3):</p> <ul style="list-style-type: none"><li>• High intake: whole grains, nuts, polyphenols, vegetables, legumes, fish, poultry, olive oil</li><li>• Low intake: red meat, cheese, sweets, fried foods, butter</li><li>• Moderate intake: wine</li></ul> | <p>Metabolites selected in the MIND signature and their association with MIND adherence</p> <table><tr><th>Metabolites</th><th>% of selection Bootstrap-LASSO</th><th>β</th></tr><tr><td>1-methylhistidine</td><td>91</td><td>-0.24</td></tr><tr><td>Myristoyl-carnitine</td><td>72</td><td>-0.25</td></tr><tr><td>5-HIAA</td><td>67</td><td>0.27</td></tr><tr><td>Betaine</td><td>66</td><td>0.15</td></tr><tr><td>Tartaric acid</td><td>46</td><td>-0.17</td></tr><tr><td>3-HHA</td><td>43</td><td>0.21</td></tr><tr><td>DHEA-S</td><td>42</td><td>-0.10</td></tr><tr><td>cyclo(L-leucyl-L-prolyl)</td><td>40</td><td>-0.12</td></tr></table> <p>β: Association coefficient with MIND diet adherence (estimated by unpenalized linear regression) for a one standard deviation increase in metabolite concentration, adjusted for age, sex, education, smoking, BMI, use of cholesterol-lowering, hypoglycemic, or antihypertensive medications, physical activity, daily energy intake, and date of blood sampling.<br/>3-HHA: 3-hydroxyhippuric acid, 5-HIAA: 5-hydroxyindole-3-acetic acid, DHEA-S: dehydroepiandrosterone sulfate</p> <p>Association between MIND metaboscore and cognitive decline status (OR [95% CI])</p> <table><tr><th></th><th>Bordeaux case-control sample (N=418)</th><th>Dijon Case-control sample (N=420)</th></tr><tr><td>Model 1</td><td>0.62 [0.43; 0.90]</td><td>0.70 [0.48; 1.02]</td></tr><tr><td>Model 2</td><td>0.61 [0.42; 0.90]</td><td>0.73 [0.49; 1.10]</td></tr></table> <p>OR estimated for the increase of one unit of MIND metaboscore (model 1 unadjusted and controlled for age, sex and education, model 2 adjusted on BMI, smoking, alcohol consumption, physical activity, diabetes, hypercholesterolemia and hypertension and controlled for age, sex and education)</p> | Metabolites | % of selection Bootstrap-LASSO | β | 1-methylhistidine | 91 | -0.24 | Myristoyl-carnitine | 72 | -0.25 | 5-HIAA | 67 | 0.27 | Betaine | 66 | 0.15 | Tartaric acid | 46 | -0.17 | 3-HHA | 43 | 0.21 | DHEA-S | 42 | -0.10 | cyclo(L-leucyl-L-prolyl) | 40 | -0.12 |  | Bordeaux case-control sample (N=418) | Dijon Case-control sample (N=420) | Model 1 | 0.62 [0.43; 0.90] | 0.70 [0.48; 1.02] | Model 2 | 0.61 [0.42; 0.90] | 0.73 [0.49; 1.10] | <ul style="list-style-type: none"><li>• First metabolomics signature of the MIND diet based on a targeted UHPLC-MS/MS platform capturing the food metabolome, and prospectively linked to cognitive decline over 12 years.</li><li>• 8 metabolites identified: 3 positive markers (betaine, 5-HIAA, 3-HHA; plant foods) and 5 inverse markers (1-methylhistidine, myristoyl-carnitine, tartaric acid, DHEA-S, cyclo(L-leucyl-L-prolyl); red meat, wine, coffee and stress pathways).</li><li>• The MIND metaboscore was associated with 37% lower odds of accelerated cognitive decline over 12 years, with a consistent trend in an independent validation cohort.</li></ul> <p>→ Once replicated across diverse populations, it could serve as a screening tool to identify older individuals at nutritional risk for cognitive decline and support personalized dietary prevention strategies.</p> | <p>(1) Morris M.C., Tangney C, Wang Y. et al, MIND diet associated with reduced incidence of Alzheimer's disease, <i>Alzheimers Dement</i>, 2015</p> <p>(2) Low D.Y., Lefèvre-Arbogast S., González-Dominguez R. et al, <i>Mol. Nutr. Food Res.</i>, 2019</p> <p>(3) Thomas A., Lefèvre-Arbogast S., Féart c. et al, <i>Association of a MIND Diet with Brain Structure and Dementia in a French Population</i>, <i>J Prev Alzheimer Dis</i>, 2022</p> |
| Metabolites                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | % of selection Bootstrap-LASSO                                                                                                                                                                                                                                                                                        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