ACETYL-L-CARNITINE SUPPLEMENTATION FOR THE TREATMENT FOR DEPRESSIVE SYMPTOMS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report
INTRODUCTION

• Depression is common and affects about 350 million people worldwide and was the second leading cause of global disability.

• Alterations of fatty acids and lipid metabolism, important contributors of neuroplasticity, often occur in depressed persons.

• Carnitine appears to modulate the activity of several neurotrophic factors, cell membranes, lipid metabolism, and neurotransmitters in nervous tissues.
ROLE OF ALC IN DEPRESSION

A recent narrative review reported that ALC may be potentially effective and tolerable option for people affected by depression, in particular who are vulnerable to adverse events from antidepressants, such as older people.

To summarize the current evidence regarding the use of ALC as anti-depressant agent

- compared to placebo (or no intervention)
- compared to common antidepressant agents.
METHODS

• Search strategy (until end 2016)
  1. RCTs, ALC, depressive symptoms.
  2. Several databases.
  3. Full texts/conference abstracts, any language.

• Inclusion/exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCTs</td>
<td>Observational</td>
</tr>
<tr>
<td>ALC (also as add-on)</td>
<td>Not validated scales for depression</td>
</tr>
<tr>
<td>Reporting data on depressive symptoms</td>
<td>No data regarding depression</td>
</tr>
</tbody>
</table>

• Outcomes/statistical analysis
  1. SMDs \rightarrow changes of depressive symptoms in ALC vs. controls.
  2. Random-effect model \rightarrow I^2 > 50% \rightarrow meta-regression/sensitivity analyses.
  3. Publication bias.
RESULTS (1): PRISMA

- Records identified through database searching (n = 721)
- Additional records identified through other sources (n = 0)
- Records after duplicates removed (n = 509)
- Records screened (n = 509)
  - Records excluded (n = 482)
    - Full-text articles excluded (n = 15):
      - no control group (n = 6)
      - no data regarding depression (n = 6)
      - no follow-up data (n = 2)
      - review (n = 1)
  - Full-text articles assessed for eligibility (n = 27)
  - Studies included in qualitative synthesis (n = 12)
    - Studies included in quantitative synthesis (meta-analysis) (n = 12)
RESULTS (2): PLC/NONE

Nine RCTs, 231 ALC vs. 236 controls; follow-up: 8 weeks

Veronese et al., Psych Med., 2017, in press
# RESULTS (2): AGE

<table>
<thead>
<tr>
<th>Group by age</th>
<th>Study name</th>
<th>Std diff in means</th>
<th>Standard error</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>older</td>
<td>Bella et al., 1990</td>
<td>-1.542</td>
<td>0.294</td>
<td>-2.119</td>
<td>-0.966</td>
<td>0.000</td>
</tr>
<tr>
<td>older</td>
<td>Fulgente et al., 1990</td>
<td>-2.259</td>
<td>0.330</td>
<td>-2.907</td>
<td>-1.611</td>
<td>0.000</td>
</tr>
<tr>
<td>older</td>
<td>Garzya et al., 1990</td>
<td>-0.923</td>
<td>0.398</td>
<td>-1.703</td>
<td>-0.144</td>
<td>0.020</td>
</tr>
<tr>
<td>older</td>
<td>Gavrilova et al., 2015</td>
<td>-1.211</td>
<td>0.344</td>
<td>-1.885</td>
<td>-0.537</td>
<td>0.000</td>
</tr>
<tr>
<td>older</td>
<td>Gecele et al., 1991</td>
<td>-2.734</td>
<td>0.526</td>
<td>-3.765</td>
<td>-1.704</td>
<td>0.000</td>
</tr>
<tr>
<td>older</td>
<td>Tempesta et al., 1987</td>
<td>-0.618</td>
<td>0.418</td>
<td>-1.437</td>
<td>0.201</td>
<td>0.139</td>
</tr>
<tr>
<td>younger</td>
<td>Hagen et al., 2015</td>
<td>-0.123</td>
<td>0.236</td>
<td>-0.586</td>
<td>0.339</td>
<td>0.602</td>
</tr>
<tr>
<td>younger</td>
<td>Malaguarnera et al., 2011</td>
<td>-0.794</td>
<td>0.256</td>
<td>-1.295</td>
<td>-0.293</td>
<td>0.002</td>
</tr>
<tr>
<td>younger</td>
<td>Rossini et al., 2007</td>
<td>-0.183</td>
<td>0.213</td>
<td>-0.600</td>
<td>0.234</td>
<td>0.391</td>
</tr>
<tr>
<td>younger</td>
<td></td>
<td><strong>-0.351</strong></td>
<td><strong>0.204</strong></td>
<td><strong>-0.751</strong></td>
<td><strong>0.049</strong></td>
<td><strong>0.085</strong></td>
</tr>
</tbody>
</table>

- **Veronese et al., Psych Med., 2017, in press**
- **NICe, France - September 20/22, 2017**
RESULTS (3): ANTIDEPR

Three RCTs, 162 ALC vs. 162 controls; follow-up: 12 weeks

Veronese et al., Psych Med., 2017, in press
## RESULTS (4): ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Study name</th>
<th>Risk ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
<th>ALC</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bersani et al., 2013</td>
<td>0.370</td>
<td>0.174</td>
<td>0.787</td>
<td>-2.582</td>
<td>0.010</td>
<td>7 / 41</td>
<td>18 / 39</td>
</tr>
<tr>
<td>Leombruni et al., 2015</td>
<td>0.077</td>
<td>0.005</td>
<td>1.262</td>
<td>-1.797</td>
<td>0.072</td>
<td>0 / 22</td>
<td>8 / 29</td>
</tr>
<tr>
<td>Zanardi et al., 2006</td>
<td>0.356</td>
<td>0.224</td>
<td>0.565</td>
<td>-4.377</td>
<td>0.000</td>
<td>18 / 99</td>
<td>48 / 94</td>
</tr>
</tbody>
</table>

**Highlighted:**

- **Risk ratio:** 0.349
- **Lower limit:** 0.236
- **Upper limit:** 0.516
- **Z-Value:** -5.282
- **p-Value:** 0.000
- **ALC:** 25 / 162
- **Controls:** 74 / 162

**ALC** Controls

**Veronese et al., Psych Med., 2017, in press**
CONCLUSIONS

• ALC supplementation appears to confer a **significant decrease in depressive symptoms** compared to placebo/no intervention.

• ALC appears to have a **similar effect to some common antidepressant agents** with significantly fewer side effects.

• The use of ALC is **safer than some traditional antidepressants** suggesting a potential role of ALC for treating depression in older people.