Erratum to

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Erratum to: Effect of GLP-1 receptor agonist treatment on body weight in obese antipsychotic-treated patients with schizophrenia: a randomized, placebo-controlled trial

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7 OPEN, Odense Patient Data Explorative Network, Odense University Hospital/ Institute of Clinical Research, University of Southern Denmark, Odense, Denmark

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The TAO study is investigator-initiated and not sponsored by pharmaceutical industry.
Dear Editor,

“Treatment of antipsychotic-associated obesity with a GLP-1 receptor agonist (GLP-1RA): The TAO trial” is the first clinical investigation of GLP-1RA treatment (exenatide 2 mg once-weekly or placebo) in antipsychotic-treated schizophrenia patients with obesity.1 Recently, we published the main results from the TAO trial as an original article in Diabetes, Obesity and Metabolism.2

We regret to report, that further analyses of the TAO dataset have revealed an error in our secondary analyses presented in the original publication. Importantly, the error did not influence the result of the primary endpoint (change in body weight) showing that both patients treated with exenatide as well as the placebo group experienced significant (P = .004), but similar weight losses of 2.24 ± 3.3 and 2.23 ± 4.4 kg (P = .98).

The error specifically relates to our secondary analyses of the metabolic blood parameters. In these analyses, the coding of ‘visit type’ had been shuffled, and in turn, the data and statistical tests of the metabolic blood parameters in Section 2.6.4 and Table 3 were based on incorrect visit types.2 Reductions in body weight are typically associated with improvement in metabolic blood parameters, and our unexpected report of a post-intervention worsening of blood metabolic parameters after 3 months, was therefore incorrect and misleading. Below, we present a corrected version of Table 3, and we present a modified Results section. Finally, we briefly discuss implications of these corrected secondary analyses.

[Insert Corrected Table 3]
Corrected Results (corresponding to the second paragraph Section 3.2 in. Changes are shown in italic font).

Plasma exenatide significantly increased in the exenatide group compared to the placebo group (P = .002) (Table 3). Exenatide treatment compared to placebo (Time × Group interaction) significantly reduced central 24-hour systolic blood pressure (P = .004) and pulse wave velocity (P = .007). A trend level Time × Group interaction was found for HbA1c (P = .063), indicating that exenatide tended to lower HbA1c compared to placebo.

Significant effects of Time were found on central 24-hour systolic blood pressure (P = .048), peripheral 24-hour systolic blood pressure (P = .03), fasting plasma glucose (P = .006), plasma exenatide (P = .002), triglyceride (P = .044), total cholesterol (P = .009), and high-density lipoprotein cholesterol (P = .006). No significant effect of Time was found on low-density lipoprotein (P = 0.289), and a trend level significant effect of Time was found for very low-density lipoprotein (P = .054). Regarding plasma exenatide, we found an effect of Group (P < .001), but no effect of Group was found for any other secondary outcomes. Post hoc correction for smoking status did not significantly change results concerning any secondary outcomes.

Implications

Regardless of treatment arm, the moderate weight loss of 2.3 kg over three months in the TAO study was associated with small reductions in fasting plasma glucose, triglyceride, total cholesterol, and high-density lipoprotein cholesterol. At trend-level significance, we observed an indication of an HbA1c lowering effect of exenatide. Interestingly, two recently published studies in antipsychotic-treated schizophrenia patients showed that GLP-1RA treatment improved blood metabolic parameters and promoted weight loss. Since one study investigated exenatide 2 mg
once-weekly in clozapine-treated patient for 24 weeks,³ and the other study used liraglutide 1.8 mg daily in pre-diabetic patients in olanzapine- or clozapine-treated patients ⁴, further research is needed to determine a potential role of GLP-1RA treatment in antipsychotic treated patients with obesity.

Comment

The reported error had minor overall impact on our study. However, the premise for progress of research is availability of accurate data, and our originally reported blood metabolic parameters were misleading. We have meticulously checked all analyses related to this study, and we confidently claim that no other mistakes are present. Please accept our sincere apologies of this unfortunate inaccuracy. May this attempt to provide transparency not compromise confidence in the presented data.
References


### Corrected Table 3. Biochemical fasting blood values

<table>
<thead>
<tr>
<th></th>
<th>Exenatide (n=20)</th>
<th>Placebo (n=20)</th>
<th>Time p-value</th>
<th>Group p-value</th>
<th>Time x Group p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c (mmol/mol)</strong></td>
<td>Baseline</td>
<td>End-of-trial</td>
<td>Baseline</td>
<td>End-of-trial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>35.95 ± 3.60</td>
<td>34.00 ± 3.39</td>
<td>35.75 ± 4.96</td>
<td>38.3 ± 13.58</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[29-42]</td>
<td>[29-42]</td>
<td>[28-47]</td>
<td>[27-93]</td>
<td></td>
</tr>
<tr>
<td><strong>Fasting plasma glucose (mM)</strong></td>
<td>5.46 ± 0.55</td>
<td>5.26 ± 0.36</td>
<td>5.71 ± 0.86</td>
<td>5.39 ± 0.44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[4.2-6.5]</td>
<td>[4.3-5.9]</td>
<td>[4.8-8.3]</td>
<td>[4.8-6.4]</td>
<td></td>
</tr>
<tr>
<td><strong>Plasma exenatide (pmol/L)</strong></td>
<td>3.4 ± 10.5</td>
<td>84.9 ± 29.6</td>
<td>0.0 ± 0</td>
<td>1.1 ± 3.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[0-40]</td>
<td>[65-147]</td>
<td>[0-0]</td>
<td>[0-11]</td>
<td></td>
</tr>
<tr>
<td><strong>Plasma glucagon (pmol/L)</strong></td>
<td>3.75 ± 13.1</td>
<td>17.8 ± 19.1</td>
<td>0.0 ± 0.0</td>
<td>0.0 ± 0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[0-58]</td>
<td>[0-50]</td>
<td>[0-0]</td>
<td>[0-0]</td>
<td></td>
</tr>
<tr>
<td><strong>Triglyceride (mmol/L)</strong></td>
<td>2.12 ± 1.07</td>
<td>1.86 ± 0.93</td>
<td>1.76 ± 0.97</td>
<td>1.63 ± 0.94</td>
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</tr>
<tr>
<td></td>
<td>[0.65-4.47]</td>
<td>[0.57-3.66]</td>
<td>[0.52-4.31]</td>
<td>[0.44-3.51]</td>
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</tr>
<tr>
<td><strong>Total cholesterol (mmol/L)</strong></td>
<td>5.04 ± 1.06</td>
<td>4.84 ± 1.16</td>
<td>4.86 ± 0.95</td>
<td>4.57 ± 0.75</td>
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</tr>
<tr>
<td></td>
<td>[3.0-7.0]</td>
<td>[2.8-7.7]</td>
<td>[2.5-6.9]</td>
<td>[3.2-6.7]</td>
<td></td>
</tr>
<tr>
<td><strong>LDL cholesterol (mmol/L)</strong></td>
<td>3.06 ± 0.86</td>
<td>3.03 ± 0.98</td>
<td>2.96 ± 0.76</td>
<td>2.82 ± 0.66</td>
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<td>[1.1-4.4]</td>
<td>[0.9-5.2]</td>
<td>[1.0-4.7]</td>
<td>[1.2-4.4]</td>
<td></td>
</tr>
<tr>
<td><strong>VLDL cholesterol (mmol/L)</strong></td>
<td>0.96 ± 0.48</td>
<td>0.83 ± 0.42</td>
<td>0.79 ± 0.44</td>
<td>0.75 ± 0.43</td>
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<tr>
<td></td>
<td>[0.3-2.0]</td>
<td>[0.3-1.6]</td>
<td>[0.2-1.9]</td>
<td>[0.2-1.6]</td>
<td></td>
</tr>
<tr>
<td><strong>HDL cholesterol (mmol/L)</strong></td>
<td>1.03 ± 0.22</td>
<td>0.98 ± 0.22</td>
<td>1.10 ± 0.31</td>
<td>1.01 ± 0.26</td>
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</tr>
<tr>
<td></td>
<td>[0.56-1.39]</td>
<td>[0.61-1.60]</td>
<td>[0.66-1.82]</td>
<td>[0.58-1.51]</td>
<td></td>
</tr>
</tbody>
</table>

Mean, standard deviation (SD) and range (in square brackets) are presented as: mean ± SD. P-values were analysed using repeated measures analysis of variance, and significant group differences are indicated by asterisks (*).

Abbreviations: HbA1c, hemoglobin A1c (<42 mmol/mol indicates normoglycemia; 42-47 mmol/mol indicates prediabetes and >48 mmol/mol indicates diabetes); HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very low density lipoprotein.