

Table 2.
Articles on Exenatide

Author	Study design	Age, y	Diagnosis	Duration	Group, n	Dose range	Scales to measure the clinical outcome	Clinical Outcome	Common side effects
Athauda et al ²⁶	Post hoc analysis of an RCT	No specific age range	Parkinson disease	60 wk	31	2 mg once weekly	NMSS, PDQ-39, MDS-UPDRS Part 1, MADRS scores	Compared to placebo, patients treated with exenatide once weekly had greater improvements in individual domains assessing mood/depression across all observer-rated outcome measures after 48 wk including the “mood/apathy” domain of the NMSS, -3.3 points (95% CI -6.2 to -0.4), $P = .026$; the “mood” score ($Q1.3 + Q1.4$ of the MDS-UPDRS Part 1), -0.3 points (95% CI, -0.6 to -0.1), $P = .034$; and a trend in the MADRS total score, -1.7 points (95% CI, -3.6 to 0.2), $P = .071$. At 48 weeks, these changes were of a magnitude that would be subjectively meaningful to patients and were not associated with changes in motor severity or other factors, suggesting exenatide may exert independent effects on mood dysfunction. The proportion of patients reporting depressive symptoms (as defined by the total MADRS score > 7) in the placebo group increased from 17% at baseline to 25% at 48 wk, while in the exenatide group, the proportion of patients reporting depressive symptoms reduced from 23% at baseline to 6% of patients at 48 wk	None reported
Angarita et al ¹⁵	RCT, crossover study	30–55	Cocaine use disorder	44 mo	13	5 μ g, 0.02 mL exenatide or placebo (saline) 3 h before cocaine administration	VAS self-ratings for subjective outcomes, number of infusions of cocaine for behavioral outcomes	Pretreatment with exenatide (8.5 ± 1.2) did not change the number of cocaine infusions in comparison to pretreatment with placebo (9.1 ± 1.2) ($F[1, 12] = 0.76$, $P = .39$). Exenatide did not change primary subjective outcomes of cocaine-induced subjective effects of euphoria/“high” (4.4 ± 0.8 vs 4.0 ± 0.8 ; $F[1, 12] = 1.73$, $P = .21$) nor wanting cocaine (5.5 ± 0.9 vs 5.4 ± 0.9 ; $F[1, 12] = 0.58$, $P = .46$), compared to placebo. Pretreatment with exenatide had an effect on levels of GLP-1 ($F[1, 55] = 4.65$, $P = .03$) and insulin ($F[1, 55] = 5.69$, $P = .02$), but not amylin ($F[1, 50] = 1.17$, $P = .28$). Both GLP-1 and insulin were lower following exenatide during cocaine self-administration (GLP-1 = 22.6 ± 3.3 pg/mL; insulin = 9.5 ± 1.4 uIU/mL) as compared to placebo during cocaine self-administration (GLP-1 = 26.6 ± 4.3 ; insulin = 13.8 ± 2.1 uIU/mL)	No adverse effects were reported

(continued)

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Klausen et al ³⁷	RCT	Mean = 52	Alcohol use disorder	26 wk	Exenatide (n = 62), placebo (n = 65)	2 mg subcutaneously once weekly for 26 wk	AUDIT, Fagerström Test for Nicotine Dependence, SF-36, Symptom Checklist-92	Exenatide did not significantly reduce the number of heavy drinking days compared with placebo. Exploratory analyses revealed that exenatide significantly reduced heavy drinking days by 23.6 percentage points (95% CI, -44.4 to -2.7, $P = .034$) and total alcohol intake per 30 d by 1,205 g (95% CI, -2,206 to -204, $P = .026$) in a subgroup of obese patients (BMI > 30 kg/m ²). The mean (SD) number of injections was 22.6 (2.2) in the exenatide group and 22.1 (2.8) in the placebo group. In patients with a BMI less than 25 kg/m ² (n = 52), treatment with exenatide increased the number of heavy drinking days by 27.5 percentage points (95% CI, 4.7–50.2, $P = .024$) relative to the placebo group	Gastrointestinal side effects were higher in the exenatide compared with the placebo group (nausea, 37.1% vs 15.4%; decreased appetite, 24.2% vs 9.2%; vomiting, 22.6% vs 7.7%; overall weight loss, 67.7% vs 40.0%; fatigue, 12.9% vs 4.6%; injection site reaction, 41.0% vs 0.0%)
Ishøy et al ²⁸	RCT	Exenatide = 19–65 vs placebo = 19–56	Schizophrenia spectrum disorder	28 mo	Exenatide (n = 20), placebo (n = 20)	2 mg once weekly	BACS, REY, SF-36, PSP, PANSS	Three-month treatment with the GLP-1 receptor agonist, exenatide 2 mg once weekly, did not improve cognition or psychosocial function in patients with schizophrenia spectrum disorder. In Short-Form 36, the parameter “functioning limitations due to emotional problems” showed an effect of “Time” ($P = .01$) and no effect of “Group” ($P = .43$), but a significant “Time × Group” interaction ($P = .02$) with exenatide treated patients scoring higher than the placebo group	Gastrointestinal side effects were reported
Mullins et al ²⁹	RCT	>60	Alzheimer disease	6 years 9 months	Exenatide (n = 13) Placebo (n = 14)	5 mcg twice daily and then after 1 wk 10 mcg twice daily	CDR, OGTT, MRI	Exenatide treatment produced no differences in clinical and cognitive measures	Nausea was reported
Eren-Yazicioglu et al ³⁰	Cross-sectional Study	18–65	Obesity with T2DM	3 mo	Exenatide 23, placebo = 20	0.01 mg twice daily	PHQ-9, GAD-7, PRT, SHAPS, CFQ, LNB, CSS, PSS, CTQ	Patients taking exenatide reported higher PHQ-9 scores (9.70 ± 4.92 vs 6.70 ± 4.66 ; $P = .026$). Patients with exenatide use also reported higher GAD-7 scores; it was not at a significant level (8.04 ± 5.69 vs 4.70 ± 2.54 ; $P = .055$). Exenatide did not show statistically significant effect on cognitive measures ($P = .066$), anhedonia, and reward learning assessment	No side effects were reported

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, BACS = Brief Assessment of Cognition in Schizophrenia, CDR = Clinical Dementia Rating, CFQ = Cognitive Failures Questionnaire, CSS = Chronic Stress Scale, CTQ = Childhood Trauma Questionnaire, GAD-7 = Generalized Anxiety Disorder-7, GLP-1 RA = glucagon-like peptide 1 receptor agonist, LNB = Letter-N-Back Task, MADRS = Montgomery-Asberg Depression Rating Scale, MDS-UPDRS = Movement Disorder Society-Unified Parkinson Disease Rating Scale, MRI = magnetic resonance imaging, NMSS = Non-Motor Symptoms Scale for Parkinson Disease, OGTT = oral glucose tolerance test, PANSS = Positive and Negative Syndrome Scale, PDQ-39 = Parkinson's Disease Questionnaire, PHQ-9 = 9-item Patient Health Questionnaire, PRT = probabilistic reward task, PSP = Personal and Social Performance Scale, PSS = Perceived Stress Scale, REY = Rey-Osterreith complex figure test, SF-36 = 36-Item Short Form Survey, SHAPS = Snaith-Hamilton Pleasure Scale, T2DM = type 2 diabetes mellitus, VAS = visual analog scale.