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Title: The relationship between oxytocin, dietary intake and feeding: a systematic review and meta-analysis of studies in mice and rats

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Abstract

The neuropeptide oxytocin has been associated with food intake and feeding behaviour. This systematic review aimed to investigate the impact of oxytocin on dietary intake and feeding behaviour in rodent studies. Six electronic databases were searched to identify published studies to April 2018. Preclinical studies in mice and rats were included if they reported: 1) a dietary measure (i.e. food or nutrient and/or behaviour 2) an oxytocin measure, and 3) relationship between the two measures. A total of 75 articles (n=246 experiments) were included, and study quality appraised. The majority of studies were carried out in males (87%). The top three oxytocin outcomes assessed were: exogenous oxytocin administration (n=126), oxytocin-receptor antagonist administration (n=46) and oxytocin gene deletion (n=29). Meta-analysis of exogenous studies in mice (3 studies, n=43 comparisons) and rats (n=8 studies (n=82 comparisons) showed an overall decrease in food intake with maximum effect shown at 2h post-administration.

Keywords: dietary intake, feeding behaviour, oxytocin, addiction, mice, rats

1. Introduction

Oxytocin is best characterised for its role in parturition, the milk-let down reflex and social bonding.[1] However, there is now significant literature supporting a role for oxytocin in other central nervous system and peripheral functions outside of these classically recognised roles. For example, oxytocin has been implicated in the regulation of a number of behaviours that are known to alter eating behaviours including anxiety, stress and social interaction.[2-4] These actions have been highlighted by investigations into the possible therapeutic role of oxytocin in several neuropsychiatric disorders including substance use disorders, and mental health disorders.[5,6] Interestingly, a role for oxytocin in food intake and feeding behaviour has also been suggested.

Oxytocin is a nine amino neuropeptide and hormone that is produced primarily in the paraventricular and supraoptic nuclei of the hypothalamus.[1] For its peripheral functions, oxytocin is released into the systemic bloodstream via the posterior pituitary gland whereby it travels to peripheral targets (e.g. uterus, gastrointestinal tract), or released from axon or dendritic terminals in specific brain regions.[1,7] Interestingly, oxytocin receptor expression is high in brain regions involved in the regulation of food intake and energy metabolism, including the hypothalamus (e.g. ventromedial hypothalamus), nucleus accumbens, amygdala, ventral tegmental area, frontal cortex, insula, and the hindbrain (nucleus tractus solitarius). [7,8]

The past decade has seen a significant number of preclinical investigations examining the effects of oxytocin on feeding behaviour in laboratory animals. Rodent studies, particularly in mice and rats, have shown that oxytocin can function as an anorexigenic

hormone with both central (i.e. intracranial) and peripheral oxytocin administration reducing food consumption, as well as sucrose[9,10] and artificial sugar (i.e. saccharin)[11] intake. Oxytocin also reduces alcohol intake[12] which has high caloric value. Further, oxytocin has been shown to influence the motivation to consume food, even under a state of satiety,[13-16] and oxytocin knockout mice show an increased preference for sucrose,[17,18] saccharin,[19] and sodium compared to wild-type controls.[20,21] In fact deletion of the genes encoding oxytocin or oxytocin receptor in mice promotes weight gain, late onset obesity and/or dysregulated glucose regulation.[22-24]

These findings in animals are only just beginning to be translated into clinical research in humans. With respect to human studies, in a recent systematic review by our group (n=26 studies) we reported that exogenous oxytocin generally has an anorexigenic effect in healthy individuals.[25] For example, intranasal oxytocin administration significantly reduced food intake and improved eating attitudes after a single dose.[25] Furthermore, exogenous oxytocin was associated with improved cognitive control of food craving, decreased approach bias towards highly palatable foods, and a reduction in hunger-driven and reward-driven food consumption.[25] Interestingly however, there was no significant change in endogenous oxytocin levels following the consumption of a test meal (e.g. high fat meal, alcoholic beverage) or after following a prescribed dietary regime for several days (e.g. high or low sodium diet).[25] Importantly the specific central and peripheral site(s) of actions through which oxytocin mediates these modulatory effects on food intake remains unclear.

The data in humans suggest that exogenous oxytocin administration may have relevance for the therapeutic control of food intake in vulnerable individuals to reduce

overeating. Therefore, we considered it important to review and assess the collective outcomes of preclinical studies in mice and rats to help inform avenues for future research in human interventions studies. Accordingly, the primary aim of this review was to investigate the impact of oxytocin function on dietary intake and feeding behaviour in rodent studies. A secondary aim was to conduct a meta-analysis of studies investigating the effects of exogenously administered oxytocin on food or nutrient intakes.

2. Methods

2.1 Search strategy

A systematic search of six electronic databases; Cochrane, CINAHL (The Cumulative Index to Nursing and Allied Health Literature), MEDLINE (Medical Literature Analysis and Retrieval System Online), EMBASE (Excerpta Medica Database), Scopus and Web of Science; was performed. Collectively these databases report that they reliably index records, from 1970 onwards. Therefore, the search was limited to articles published in English from 1970 to April 2018. The key search words and terms are available through Supplementary material. Additionally, to ensure no relevant studies were missed a manual search of the reference lists of included studies and relevant publications was conducted.

2.2 Study criteria

Preclinical studies in mice and rats (≥6 weeks of age) were included if they met the following inclusion criteria: 1) an outcome measure related to dietary intake (i.e. food or nutrient; including alcohol, an energy producing macronutrient which contributes

to dietary energy intake) and/or behaviour (e.g. meal consumption patterns), 2) an outcome measure of oxytocin, and 3) the relationship between the two measures. Reasons for study exclusion were: studies with a non-experimental design; studies conducted in humans or animals other than mice or rats; studies focusing on pregnant or lactating female rodents; animal models with naturally occurring or artificially induced health conditions/diseases known to alter oxytocin function (e.g. pituitary gland disorders); experiments where dietary behaviours were artificially induced (e.g. treatment with angiotensin or furosemide to induce salt appetite; treatment with phenylpropanolamine to induce anorexia, use of gavages in anaesthetised rodents); and experiments using combined treatment interventions (e.g. oxytocin + leptin; oxytocin + cholecystokinin). To maintain homogeneity of the outcomes, studies examining metabolic parameters (e.g. energy expenditure) were not included in the present review. The review methodology was prospectively registered in International prospective register of systematic reviews (PROSPERO, Registration number: CRD42016053015) and follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[26]

2.3 Study selection

After the removal of duplicates, studies conducted in humans and those focusing on pregnant or lactating female rodents were excluded (JS). The identified studies were initially screened based on their title and abstracts by two independent reviewers (JS and EJC). Full text articles were then assessed for eligibility (JS, EJC and TB) with discrepancies decided by discussion using a third reviewer (CD or TB). Consensus was reached for all included studies.

2.4 Data extraction

Studies were initially categorised by the oxytocin outcome measure. Data extraction was performed by one author (JS), using a standardised table developed for this review (Tables 1-7), and cross checked independently by one other author (EJC). The extraction tool was pilot tested on six randomly selected included studies and refined by author consensus to ensure all relevant data was being captured. For studies where outcome data was not reported numerically, and instead displayed graphically, graphs were exported to an online web digitiser program (WebPlotDigitizer,[27] available from http://arohatgi.info/WebPlotDigitizer/) to obtain mean and standard deviation (SD) or standard error of the mean (SEM). This was completed for seven exogenous studies (full details in Supplementary material). Previously published literature has shown the WebPlotDigitizer is an effective method to collect data with high levels of intercoder reliability and validity.[28]

2.5 Data Synthesis and Meta-analysis

Results of the systematic review are presented in as a narrative analysis to describe the included studies. For a more rigorous analysis of experiments administering exogenous oxytocin a meta-analysis was conducted. Specific principals which have been previously published for meta-analysis[29] in pre-clinical studies were followed, including using the lowest value where a range of animals was reported for a group. For studies reporting food intake (grams) as an outcome at time points following oxytocin administration, oxytocin dose and the administration site, meta-analyses was performed with R statistical software[30] using the metafor package[31] (Version r x 64 3.5.1) and completed separately for mice and rats. For each study, an effect size

(Hedge's g, which includes a correction factor for small sample size bias) and corresponding 95% confidence intervals were calculated as the standardized mean difference between the two treatment conditions (oxytocin and vehicle). To account for multiple measures per study a series of multilevel models were investigated with nested random effects for study, administration site (central or peripheral), dose (because this could not be reliably converted into standardised concentrations) and time, using REML estimation. Two fixed effect moderator variables, administration site (central or peripheral), and time (as a categorical variable, and also treated as continuous, in separate models), were included with the random effects above to form a mixed effects meta-regression models. Model comparisons using Likelihood Ratio Tests were used to determine if random effects were significant and if not important the models were simplified by removing them. Residual plots were used to examine homogeneity of variance and normality. To assess for publication bias, funnel plots were produced and visually inspected. [Dataset and R script are available in supplementary material].

2.6 Quality of Evidence

The quality of the included studies was reviewed independently by two authors (JS and EJC) using the SYRCLE risk of bias tool, scoring internal and external validity for each study.[32] The tool has ten domains, and for each domain studies were rated as either "yes" indicating a low risk of bias; "no" indicating a high risk of bias; or "unclear" if insufficient details had been reported. No studies were excluded based on quality ratings.

3. Results

3.1 Description of Studies

The search strategy, summarised in Figure 1, identified 2314 potentially eligible articles after exclusion of duplicates. After the removal of studies not meeting the inclusion criteria, the search strategy yielded 972 articles for screening. No additional articles were identified in the reference search. Initial screening of title and abstracts identified 149 articles that received a detailed assessment of the full text articles. A total of 74 studies were excluded, the major reasons for exclusion were: non-experimental study design (n=22) and wrong intervention (n=22). A total of 75 articles (n=246 experiments) are presented in the current review.

3.2 Study characteristics

A total of 246 experiments were performed in mice (n=93) and rats (n=153), between 1989 and 2018 (Tables 1-7). Experimental sample sizes ranged from 4 to 108. The exact number of rodents was not specified in 38 experiments,[10,11,14-16,23,33-46] but rather given as a range. Sample sizes were not reported in four experiments.[36,47,48] Two hundred and fourteen (87%) of the included experiments were performed in males exclusively, 19 in females exclusively and 13 in both males and female rodents. Experiments were conducted in 16 different countries, with the majority performed in USA (45%), followed by New Zealand (24%) and Sweden (8%). Most experiments (n=174) were conducted under a 12:12 light/dark cycle and 72 experiments [10-12,16,34-38,40,44,46,47,49-58] performed dietary intake measurements solely during the dark phase (i.e. the time of day a rodent would typically consume food). Short-term (≤24 hours) test durations (n=144) ranged from 10 min to 24 hours (median 120 min) and longer

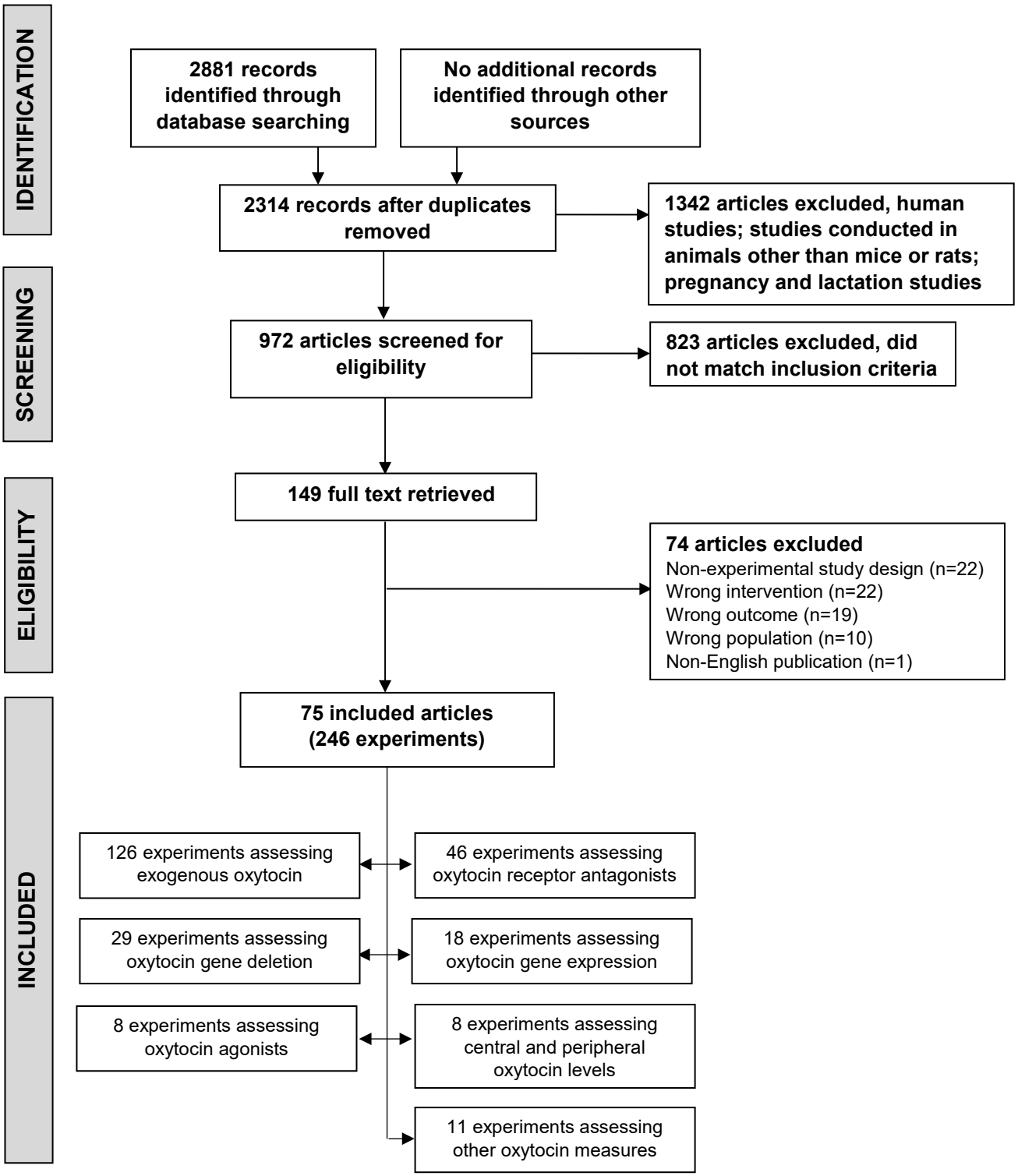


Figure 1. Flow diagram of article identification retrieval and inclusion for this systematic review

term (>24 hours) durations (n=102) ranged from 42 hours to 10 months (median 7 days). Test durations in 20% of experiments lasted longer than five days. During experimentation, the majority of animals were individually housed (n=218) except for 15 experiments, where animals were housed in pairs (n=3 experiments, employed a social context design)[11,48,59-61] or 4-6 per cage.[53,62,63] Details of housing numbers were not reported for 20 experiments.[9,22,33,55,56,58,64]

3.3 Oxytocin measures

Various oxytocin measures were used and experiments were subsequently grouped into one of the following seven categories for analysis: 1) exogenous oxytocin administration (n=125[9-11,13-16,33,36-38,40,45-47,49-52,55,58,59,62-75]); 2) oxytocin receptor antagonist administration (n=46[11,13,14,34-36,39,42,44,45,48,61,62,64,70,71,76]); 3) oxytocin gene deletion (n=29[17-23,77-81]); 4) oxytocin gene expression (n=19[11,35,41,42,48,61,74,75,82-88]); 5) oxytocin agonist administration (n=8[39,70]); 6) central (n=1)[43] and peripheral oxytocin concentrations (n=7[16,38,45,60,86,89]); and 7) other oxytocin measures (oxytocin receptor overexpression, n=2[90]; oxytocin receptor knockdown, n=3[56]; oxytocin receptor neuron activation, n=4[54]; oxytocin neuron lesions, n=1[91]; and oxytocin antisense, n= 1[89]).

3.4 Dietary characteristics

Dietary characteristics examined in relation to oxytocin measures, in descending order, included the intake (measured as grams, g/kg, mL or kcal) of and/or exposure to: overall food intake (n=92[11,13-16,22,23,33,34,36-38,42,44-46,48-51,54-56,58,59,62,63,65-70,73-77,91,92]), carbohydrates (n=45; sucrose,[9-12,17,18,35,48,61,71,73-75,78,82-84,88] glucose,[35,64] fructose,[35] polycose,[18,35] and cornstarch[18,35]), high fat diet (n=32[16,38,45,55,57,58,73,85]), sodium (n=16[20,21,54,65,79-81,86,89]), non-carbohydrate sweetener (saccharin, n=20[11,16,19,35,47,73-75]),

alcohol (n=14[12,40,47,72,87,90]), Intralipid emulsion, n=2[48,78], palatable solution [i.e. high in sodium and fat (n=1[81])], liquid only diet (Ensure nutrition drink, n=1[54]), and soya isoflavones (n=1[60]). Dietary behaviours examined in relation to oxytocin measures included: meal durations or time spent feeding (n=9[13-16,56,70]), latency to first meal (n=7[13-16]), nutrient/taste preferences (n=3[9,18,90]), food/sucrose reinforced classical and operant conditioning (n=7[10,52,69]), food/sucrose intake in familiar vs. social settings and novel environments (n=9[11,39,61]), food deprivation (n=8[53,75]) and fasted vs refed states (n=4[41-43]). In nine experiments, conditioned taste aversion and kaolin consumption were used to evaluate any potential aversive drug effects (e.g. nausea, malaise and concomitant anorexia) associated with oxytocin administration.[11,16,46,50,57,73,74] Across all the included studies the most common secondary outcome measures examined were, in descending order, body weight (n=40), appetite hormones and blood parameters (n=13), water intake (n=8), natriuresis and osmolality and (n=7), locomotor activity (n=7) and grooming behaviour (n=3).

3.5 Quality of the included studies

Risk of bias evaluation of the 75 included articles in this review is reported in Figure 2 (full details in Supplementary material). For three of the 10 domains (i.e. selection bias 2, reporting bias and other biases) the quality of the included articles were assessed as having a low risk of bias for the majority of articles (97%). For five domains, the overall quality of the included articles (97%) were assessed as having an unclear risk of bias due to the lack of detailed information regarding allocation concealment, random housing, blinding of assessors to interventions and outcomes. There was an unclear risk of attrition bias in 52% of studies with the number of animals not accounted for

both before and after experimentation. In 65% of studies, animals were not randomly allocated to the experimental and control groups (i.e. absence of sequence generation) indicating a high risk of selection bias. Baseline characteristics of animals were comparable between experimental and control groups in all studies.

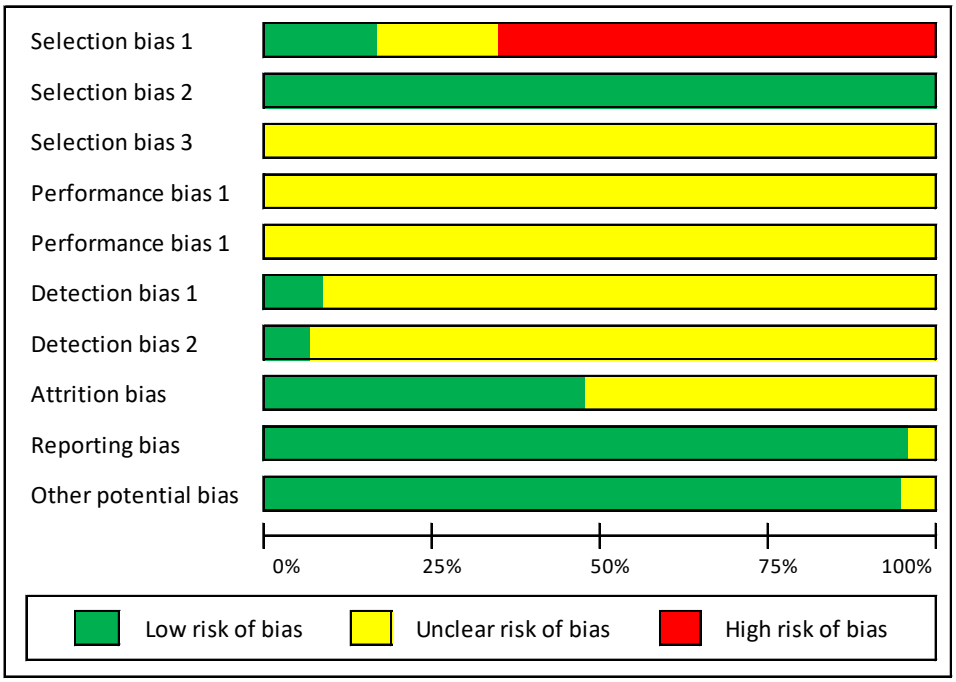


Figure 2. Risk of bias assessment of the 75 studies included in this systematic review. For each domain, studies were rated as either "yes" indicating a low risk of bias; "no" indicating a high risk of bias; or "unclear" if insufficient details had been reported.

3.6 Studies assessing the effect of exogenous oxytocin administration on dietary intake and behaviour

The majority of experiments included in this review reported the effects of exogenous oxytocin administration on dietary intake (n=114) and behaviour (n=19); Table 1.

Ninety-one were performed in rats and 34 in mice. The most frequent strain of rodent used was Sprague-Dawley rats (n=71 experiments) and C57BL/6 mice or C57BL/6 substrains (n=32 experiments). In 30 experiments, rodent models with the following pre-existing traits were included: diet-induced obese (DIO) mice/rats (n=25),[16,38,45,55,57,58] diabetic and leptin resistant mice with (n=1, B6.V-Lepob/JRj mice[33]) and without obesity (n=2, BKS db/db mice[50]), obese rats with defective leptin signalling (n=1, Zucker rats[59]; n=1, Koletsky rats[38]) and rapidly growing rats (n=1).[62] Sample sizes ranged from 6 to 108, and 20% of experiments utilised a cross-over design. Experimental durations ranged from 1h to 28 days. Administration route, site, and dose of oxytocin are reported in Table 8. Injections and intranasal oxytocin administration occurred up to 120min prior to feeding, and post-treatment dietary measurements ranged from 0.5-24 hours. Measurements of dietary intake/behaviour while rodents were receiving central or peripheral infusions of oxytocin ranged from 2 h to 28 days. The majority of experiments (n=115) administered saline as the control or vehicle dose, six used artificial cerebrospinal fluid (aCSF),[45,46,70] three used distilled water[65-67] and in one experiment[10] the type of vehicle used was not reported.

Centrally and peripherally administered oxytocin (n=52 experiments) was found to have no significant effect on food intake (standard chow) in 11 experiments,[49,58,65-68] but significantly reduced overall intake of standard chow in the majority of studies (n=37 experiments[11,13-16,33,36-38,45,46,50,51,59,62,63,70,73-75]). Six experiments reported decreases in food intake (standard chow) ranging from 19 to 66% in the 1-18h post-administration period,[11,15,38,46] with greater reductions reported within the first hour (50-66%[15,46]). In contrast, Bjorkstrand et al.[49] found in four experiments that oxytocin treated rats ate significantly more standard chow than saline treated rats. Altirriba et

al.[33] found during their 14 day trial in obese (diabetic and leptin resistant) and lean mice that the effects of chronic subcutaneous (SC) infusion of oxytocin on reducing intake of (standard chow) was only significant on day 1 in lean mice. Whereas, in obese mice maintained on the same standard chow diet as their lean counterparts, effects were sustained for 14 days with more marked effects during the first week.[33] Similarly, Roberts et al.[57] found chronic 3V oxytocin administration in mice and rats, and 4V administration in rats, produced no sustained effect on energy intake in chow fed lean rodents, but produced a sustained effect on the of reduction of food intake (~2-3 weeks) in high fat diet-fed DIO mice and rats. Blevins et al.[16] and Maejima (2011) et al.[55] reported reductions in food intake in DIO rats during the chronic treatment period were largely transient. Zhang et al.[45] found in DIO mice, twice daily (AM vs. PM) central injections of oxytocin significantly decreased both daytime and night-time food intake (high fat diet) similarly, whereas twice daily peripheral administration had a more marked effect on daytime intake. Oxytocin was found to increase the latency to begin feeding and reduce meal durations in both hungry and sated animals (6 of 6 experiments in rats).[13-16] Oxytocin had no effect on hunger or reward-driven food intake (standard chow, sucrose or saccharin) when rats were placed in a social setting (n=2).[11] During choice, no-choice and operant self-administration feeding paradigms, the administration of oxytocin had no effect on low sodium diet (n=1)[65] or glucose intake (n=1)[64]; IP and intracranial injections of oxytocin decreased sucrose (8 of 17 experiments)[9-12,52,71,74] and saccharin (2 of 9 experiments)[11] intake in fasted and non-fasted rodents. In obese and lean rodents exposed to a chow diet higher in fat (~60% kcal from fat) than standard chow (~13% kcal from fat), intracranial infusion and SC infusion or injection of oxytocin reduced energy intakes in 11 of 15

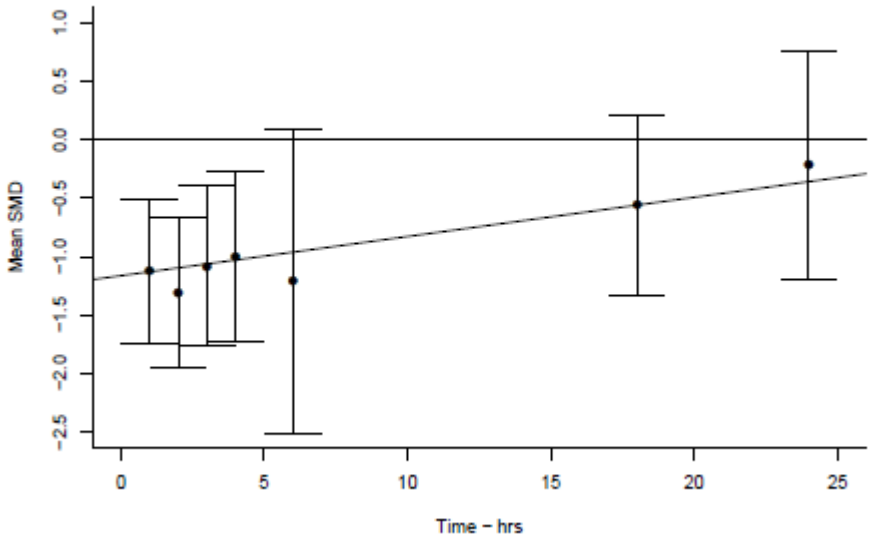
313 experiments.[16,55,57,58] Oxytocin had no effect on the intake of a palatable high fat
314 emulsion (n=1).[55] Klockars (2017a) et al.[73] found oxytocin did not shift rats' preference
315 from sucrose to high fat emulsion when given a two-bottle choice test. Oxytocin
316 decreased alcohol intake in 10 of 11 experiments,[12,40,47,72] with two experiments
317 reporting that decreases in intake ranged from 30 to 40% in the 1-2.5h post-
318 administration period.[47] Peters (2012) et al.,[40] found oxytocin had no effect on stress-
319 induced alcohol consumption (n=2). Sinclair et al.[9] found tastes response to both
320 aversive (bitter, sour and salty) and appetitive (sweet and umami) stimuli were
321 depressed following oxytocin injection. No aversive drug effects were found across
322 nine experiments evaluating kaolin intake and conditioned taste aversion associated
323 with oxytocin administration.[11,16,46,50,57,73,74] In summary, the findings from the
324 majority of experiments indicate acute doses of oxytocin are effective in reducing food
325 (both standard chow and chow higher in fat), carbohydrate and alcohol intakes.
326 Chronic treatments were more effective in producing sustained reductions in food
327 intakes in obese rodents.

328 *3.6.1 Meta-analysis results*

329 The meta-analysis (forest plot available in supplementary material) for rats (8 studies,
330 n=82 comparisons) was based on a multilevel mixed effects model to account for
331 correlation resulting from replicate experiments. Three nested factors (i.e. study,
332 administration site and dose) were found to be important and formed the random
333 effects part of the model. The fixed effects part of the model was used to examine the
334 effect of two moderators, administration site (central and peripheral), not significant
335 (p=0.26); and time since meal (chow) presentation, significant (p=0.02, treated as a

categorical variable and intercept term in the model). Time was also examined as a continuous variable, p=0.001. The final model was simplified to only contain the time effect, either in its continuous form or categorical form. For the categorical version of time, the fitted model means (no intercept term in the model, p=0.001) and 95% confidence intervals are shown in Figure 3, with the line of best fit for continuous time effect from the alternative model representation overlaid over the mean effects. The first four mean differences for 1, 2, 3 and 4h respectively are all significantly lower than zero with the 95% confidence intervals not containing zero. The 6h mean difference is similar, but is not significantly different to zero, and as it is only based on one record and has poor power. At the longer time periods of 18h and 24h the mean differences are not significantly different to zero.

The meta-analysis (forest plot available in supplementary material) was repeated for mice (3 studies, n=43 comparisons; all injections given peripherally). The final model, containing only the time effect (other factors not significant), on food intake following oxytocin administration, was not significant when treated as a continuous variable (with intercept term in the model, p=0.21). When time was examined as a categorical variable (no intercept term in the model, $p<0.001$) the mean differences for 1, 2, 3 and 6h are all significantly lower than zero with the 95% confidence intervals not containing zero. At 24h the mean difference is not significantly different to zero (Figure 4).



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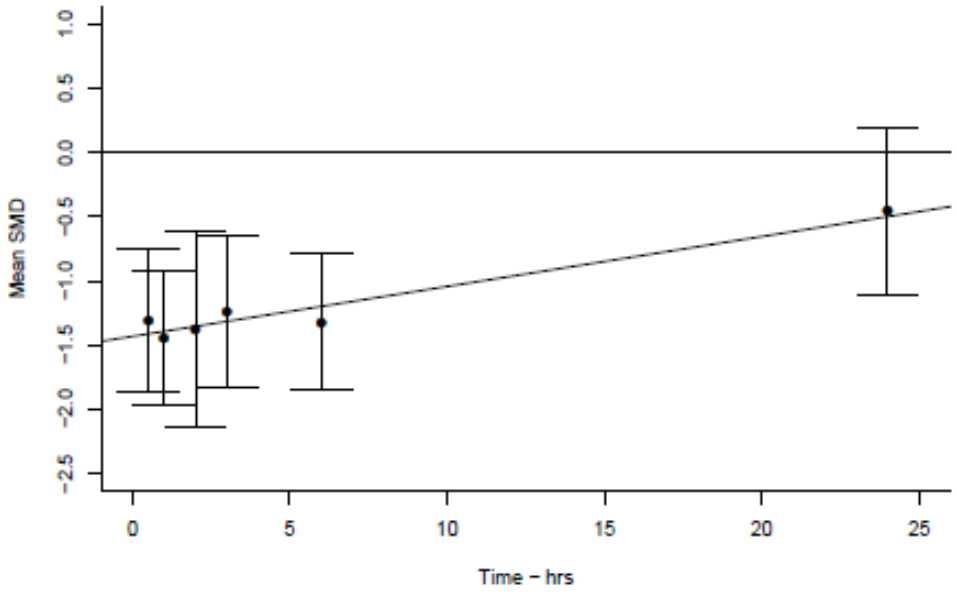
357 **Figure 3.** Multilevel mixed effects meta-analysis. Results of 8 studies (n=82
358 comparisons) in rats of the mean effect of acute oxytocin administration compared
359 with control treatment on cumulative food intake (standardised mean difference and
360 95% confidence interval) over time (hours). The vertical line through zero represents
361 the line of no treatment effect (overlaid with the line of best fit for continuous time
362 effect). Food intake was significantly reduced by oxytocin treatment at 1, 2, 3 and 4
363 hours ($p=0.0004$, $p<.0001$, $p=0.0021$, and $p=0.007$, respectively); no significant effect
364 at 6, 18 and 24 hours ($p=0.07$, $p=0.16$, and $p=0.67$, respectively).



365

366 **Figure 4.** Multilevel mixed effects meta-analysis. Results of 3 studies (n=43
367 comparisons) in mice of the mean effect of acute oxytocin administration compared
368 with control treatment on cumulative food intake (standardised mean difference and
369 95% confidence interval) over time (hours). The vertical line through zero represents
370 the line of no treatment effect (overlaid with the line of best fit for continuous time
371 effect). Food intake was significantly reduced by oxytocin treatment at 0.5, 1, 2, 3 and
372 6h ($p<0.0001$, $p<0.0001$, $p=0.0004$, $p<.0001$, and $p<.0001$, respectively); no significant
373 effect at 24 hours ($p=0.17$).

374 *Bias.* Within each study the original effect sizes were affected by time (as a
375 moderator). Therefore to test for potential bias, residuals were used in funnel plots as
376 these have been adjusted for the mean values for each of the time periods. The
377 funnel plots (supplementary material) associated with each meta-analysis (rats or
378 mice) show some degree of asymmetry. Rank correlation test for rats (Kendall's tau = -
379 0.3111, $p < 0.0001$) and mice (Kendall's tau = -0.5216, $p <0.0001$) indicate bias may be
380 present. The asymmetry in the funnel plots shows more negative effects associated

with larger standard errors which indicates that studies with positive effects are likely not being published. This may be for smaller studies that have lower sample sizes (or more variable studies).

3.7 Studies assessing the effect of oxytocin receptor antagonists on dietary intake and behaviour

Forty-six experiments assessed the effect of oxytocin receptor antagonists on dietary intake and behaviour (Table 2), 33 were performed in rats and 11 in mice. Sample sizes ranged from 6 to 51, and five experiments utilised a cross-over design. Experimental durations ranged from 10min to one week. Oxytocin receptor antagonists administered included [d$(CH_2)_5^1$, Tyr(Me)^2, Orn8]-OT; L-368,899; [1-(3-mercaptopropionic acid), 2-0-ethyl-D-Tyr, 4-Thr,8_Orn]-OT; 1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin; [d$(CH_2)_5$,Tyr(Me)2,Orn^8] vasotocin and non-penetrable L-371,257. One study[44] did not report the antagonist used. Routes of oxytocin receptor antagonist administration included: ICV (n=1) or SC (n=1) infusions for 3 to 5 days; intraperitoneal injection (IP; n=14); intracranial injections [intracerebroventricular, n=9 (lateral ventricle, n=8; third ventricle, n=2; fourth ventricle, n=2); ventral tegmental area, n=3; ventromedial, n=3; nucleus accumbens core, n=2; basolateral and central nuclei of the amygdala, n=4]; and SC or intravenous injections (IV; n=6). Oxytocin receptor antagonist doses administered via osmotic pump infusions were 40µg/h^{-1}/kg (SC delivery) and 1µg/rat (lateral ventricle delivery). IP injection ranged from 0.1 to 30mg/kg; intracranial injections ranged from 0.3 to 10mg/kg, or 0.1 to 10µg, or 1 to 3µl or 0.8 to 20nmol; SC dose of 1.5mg/kg; and IV injections of 1.0µg or 30µg/kg. Injections occurred up to 45min prior to feeding, and post-treatment measurement of

404 dietary intake/behaviour ranged from 30min to 7 days. All experiments included a
405 vehicle dose, either saline (n=42) or aCSF (n=4), and 14 experiments compared the
406 effect of oxytocin to oxytocin receptor antagonist.[11,13,14,36,44,62,64,70,71] In 18
407 experiments, rodents were pre-treated with an oxytocin receptor antagonist before
408 the administration of oxytocin.[11-14,36,44,62,64,70,71,73-75]

409 Central and peripheral administration of oxytocin receptor antagonist significantly
410 increased overall food intake compared to vehicle in six experiments,[13,14,34,36,45,92] but
411 was found to have no significant effect in five experiments.[42,48,62,75,76] Baskin et al.[34]
412 reported food intake of treated rats increased by 77% in the 4h post administration
413 period compared to vehicle. Olson (1991a) et al.[70] found high doses (20nmol) of
414 oxytocin receptor antagonist inhibited food intake. Eleven experiments found the
415 anorexigenic action of oxytocin on food intake, including the latency to consume and
416 consumption duration, was counteracted by pre-treatment with an oxytocin receptor
417 antagonist.[11,13,14,36,44,70,73-75] Ho et al.[36] reported the systemic administration (IP) of a
418 non-penetrant oxytocin receptor antagonist attenuated the inhibitory effects elicited
419 by fourth ventricular administration of oxytocin. Zhang et al.[45] found twice daily (AM
420 vs. PM) central oxytocin receptor antagonist injections increased daytime and night-
421 time food intakes significantly, with a more marked effect on daytime intake, whereas
422 twice daily peripheral administration affected daytime intake only. During choice and
423 no-choice feeding paradigms, when compared to controls, oxytocin receptor
424 antagonist treated rodents in 15 of 17 experiments had increased intakes of
425 carbohydrates: sucrose (n=10[11,35,48,71]), glucose (n=2[35,64]), polycose (n=2[35]), cornstarch
426 (n=2[35]) and fructose (n=2[35]); and non-carbohydrate saccharin (n=2[11,35]). Pre-treatment
427 with an oxytocin receptor antagonist was found to abolish the anorexigenic effect of

oxytocin on sucrose, glucose and saccharin (n=8[11,64,71,73,74]); alcohol (n=1[12]) and palatable fat intake (Intralipid emulsion, n=1[73]). Oxytocin receptor antagonist treatment when given alone had no effect on Intralipid emulsion intake (n=1[48]). When mice were presented concurrently with palatable lipid and sucrose solutions (n=1[48]), or saccharin and sucrose solutions (n=1[35]) mice consumed more sucrose. Olszewski (2015) et al.[61] found that when dominant and subordinate mice were treated with an oxytocin receptor antagonist, dominant mice consumed increased amounts of sucrose in both non-social and social contexts, whereas subordinate mice only consumed more sucrose in the non-social environment. In summary, the majority of experiments found acute and chronic administration of penetrable oxytocin receptor antagonists increased intakes of food (i.e. standard chow, carbohydrates, saccharin and alcohol), with the exception of Intralipid emulsion. Antagonist administration, prior to oxytocin treatments, counteracted oxytocin's anorexigenic effects, on food intakes including Intralipid emulsion.

3.8 Studies assessing the effect of oxytocin agonists on dietary intake and behaviour

Eight experiments assessed the effect of oxytocin agonists on dietary intake and behaviour (Table 3). Four experiments, conducted by Olson (1991a) et al.,[70] assessed the effect of ICV administered oxytocin agonist (e-L-β-MePhe^2) on food intake (n=3) and time spent feeding (n=1) in Sprague-Dawley rats. Sample sizes ranged from 5-16 and three experiments utilised a cross-over design. Agonist doses ranged from 10-500pmol and were administered just prior to feeding. Overall food intake and time spent feeding was significantly decreased in the 60min following agonist administration (all doses). Olson et al. (1991a) reported that rats developed a

tolerance to the agonist's inhibitory effects by day three and food intake returned to baseline levels. In one experiment, it was found that pre-treatment with an oxytocin receptor antagonist [$(CH_2)_5^1$,Phe(Me)^2,Thr^4,Orn^8] abolished the inhibitory effects of [e-L-β-MePhe2]oxytocin on food intake.[70] Oxytocin agonist administration had an opposite effect on food intake when administered in rodents with hyponeophagia (feeding inhibition induced by a novel environment).[39] Four experiments, conducted by Olsewski (2014) et al.,[39] assessed the effect of IP administered oxytocin agonist (WAY-267,464), on reward and hunger driven food intake in novel and familiar (home cage) environments in BALB/c mice. Sample sizes ranged from ~24 to ~36, and agonist doses administered just prior to feeding ranged from 10 to 500pmol. Oxytocin agonist administration did not alter food intake in mice fed standard chow in familiar settings, though it reduced the inhibition of feeding produced by a novel environment. This included a reduced latency to approach palatable food (sweetened condensed milk) and an increase in food intake. The decrease in anxiety hyponeophagia was abolished by pre-treatment with an oxytocin receptor antagonist (L-368,899).[39] In summary, when rodents were fed in a familiar environment, food intake was generally reduced following agonist administration. Whereas when rodents were fed in a novel environment, the usual suppression of food intake induced by an unfamiliar setting was ameliorated, and food intake increased.

3.9 Studies assessing the effect of oxytocin gene deletion on dietary intake and behaviour

Twenty-eight experiments assessed the effect of oxytocin gene deletion on dietary intake and behaviour in male (n=18) and female mice (Table 4). Sample sizes ranged

474 from 10 to 28 and the most frequent strain of oxytocin knock out mice (OT KO) used
475 were derived from C57BL/6 mice (n=24 experiments). Two experiments compared
476 ovariectomised OT KO and wild type mice (WT) to intact controls.[79] Choice and no-
477 choice feeding paradigms were used and testing durations of experiments ranged
478 from 3 days to 5 weeks. Across the 11 experiments assessing sweet solution intake, OT
479 KO mice displayed a significant increase in and sustained preference for sucrose
480 (n=9[17,18,78]) and saccharin (n=2[19]) compared to WT mice. There was no significant
481 difference in intake between genotypes when fed standard chow alone (n=2[22,77]) or
482 high fat vs standard diet (n=1[23]). When given a series of two-bottle choice tests,
483 Scalfani et al.[18] found OT KO mice consumed greater amounts of both sweet and non-
484 sweet carbohydrate solutions (i.e., sucrose, polycose, and cornstarch) compared with
485 WT cohorts, but there was no difference in their intake of a palatable lipid emulsion. In
486 four experiments, Miedlar et al.[78] found OT KO mice consumed significantly more
487 palatable lipid emulsion than WT on day one only, but there was no difference in
488 overall 3-day intake between genotypes. Similarly, Vollmer (2013) et al.[81] found during
489 a 4-day exposure to a palatable solution, high in sodium and fat, all mice consumed
490 large amounts with no significant differences between genotypes.[81] In two-bottle
491 preference tests (n=7[20,21,79-81]) in which mice could choose between water or a sodium
492 chloride solution (NaCl), OT KO mice consumed significantly greater amounts of NaCl
493 then WT mice in five[20,21,79] of the seven experiments. In a two-diet choice test (low vs.
494 high sodium chow) there was no difference in intake between OT KO and WT
495 cohorts.[81] In summary, oxytocin KO mice displayed a preference for carbohydrate,
496 saccharin and sodium solutions, compared to their WT counterparts. Oxytocin gene

deletion had no significant effect on the consumption of chows, with varying macronutrient profiles, or Intralipid emulsion.

3.10 Studies assessing the effect of dietary intake and behaviour on oxytocin gene expression

Nineteen experiments assessed the effect of dietary intake and behaviour on oxytocin gene expression and hypothalamic oxytocin levels (Table 5). Short-term exposure (<24h) to sucrose (n=2[82,83]) had no effect on gene expression, whereas longer term exposure (≥24h to 42 days) to sucrose (n=6[35,48,61,83,84,88]), cornstarch (n=2[35,83]) or palatable lipid solutions (n=1[48]) increased oxytocin mRNA levels (n=5[35,48,61,84]) and activated oxytocin neurons (assessed using the Fos-protein marker) (n=3[48,83,88]). Prolonged high fat diet (11 weeks) in ovariectomised mice (n=1[85]) produced negligible Fos expression in oxytocin neurons in the paraventricular nucleus (PVN) of the hypothalamus. Olszewski (2010) et al.[48] found when mice were grouped according to sucrose or fat preference, baseline oxytocin mRNA levels did not differ between 'sucrose preferrers' and 'fat preferrers'. Further, Olszewski (2010) et al.[48] examined hypothalamic oxytocin gene expression in dominant and subordinate mice (dyads) consuming sugar, and found oxytocin mRNA levels were higher in dominant mice. Forty-eight hour exposure to saccharin had no effect on oxytocin mRNA levels in one experiment,[35] whereas in another experiment a decrease in gene expression was reported.[11] Shorter term exposure (2-24h) to saccharin significantly upregulated oxytocin receptor mRNA expression in the central nuclei of the amygdala (CNA; n=1[74]), but had no effect on the basolateral nuclei of the amygdala (BLA; n=1[74]); or on ventromedial hypothalamic nuclei (VMH; n=1[75]). Prolonged alcohol exposure (6-10

520 months) decreased the number of oxytocin neurons, but had no effect on mRNA
521 levels.[87] Following a fasting-refeeding regime, Uchoa et al.[42] found refeeding increased
522 the number and percentage of Fos-positive oxytocin neurons in the PVN and
523 supraoptic nucleus (SON) of the hypothalamus, but did not alter oxytocin mRNA
524 expression in these regions (experiment 2). Suyama et al.[41] found increased synaptic
525 input onto PVN oxytocin neurons in ad libitum fed compared to the fasted state.
526 Oxytocin receptor mRNA was increased by food deprivation in the VMH (n=1[75]) and
527 CNA (n=1[74]), but not in the BLA (n=1[74]). Salt loading (replacement of drinking water
528 with 2% sodium chloride) in rats produced a significant elevation in oxytocin gene
529 expression in the SON (n=1).[86] In summary, upregulation of oxytocin mRNA levels
530 occurred largely in response to chronic carbohydrate exposure, compared to standard
531 chow, saccharin or Intralipid emulsions.

532 *3.11 Studies assessing the effect of dietary intake and behaviour on peripheral and*
533 *central oxytocin concentrations*

534 Eight experiments assessed the effect of dietary or nutrient intake on central
535 (hypothalamic nuclei, n=3[43,45,89]) and peripheral (plasma, n=5[38,45,53,60,86,89]) oxytocin
536 concentrations (Table 6). Plasma oxytocin levels were unaltered in rats fed high fat
537 diets compared to controls (n=1[38]), whereas the diurnal rhythmicity in 24-hour peak
538 circulating plasma oxytocin levels (n=1[45]) and hypothalamic oxytocin release (n=1[45])
539 was abolished in mice fed a high fat diet. Morris et al.[89] found a high intake of salt (i.e.
540 salt loading) increased plasma oxytocin in baroreceptor-denervated rats, but not in
541 healthy controls (sham operated). In contrast, Greenwood et al.[86] found salt loading
542 increased plasma oxytocin levels in healthy rats. Exposure to a high soya isoflavone

543 diet had no effect on plasma oxytocin concentrations (n=1).[60] Food deprivation
544 produced no significant change in oxytocin concentrations in plasma (n=1[53]), or in
545 hypothalamic nuclei, with the exception of the median eminence (n=1[43]). This effect in
546 the median eminence was not significantly reversed by refeeding. In summary,
547 alterations in endogenous oxytocin concentrations occurred in response to sodium
548 and chronic high fat diet intakes, and food deprivation.

549 *3.12 Studies assessing other measures of oxytocin on dietary intake and behaviour*

550 Of the 11 experiments assessing other measures of oxytocin (Table 7), two
551 experiments conducted by Bahi et al.,[90] examined the effect of increased expression of
552 the oxytocin receptor, in the nucleus accumbens, on voluntary alcohol consumption
553 and taste sensitivity. Oxytocin receptor overexpression, relative to sham controls, led
554 to a decrease in voluntary alcohol consumption. The same mice, when exposed to
555 sweet and bitter tastants (i.e. saccharin and quinine), showed similar intake and
556 preference for both tastants. Ryan (2017) et al.[54] found chemogenetic activation of
557 oxytocin receptor neurons (n=2) in the parabrachial nucleus of the pons in mice did
558 not decrease usual food intake, or food intake (standard chow or liquid diet) after
559 fasting, but did decrease sodium intake in dehydrated mice. Overall, Ong (2017) et
560 al.[93] found virally mediated oxytocin receptor knockdown had no significant effect on
561 food intake in fasted or satiated rats (n=3). Wu et al.[91] found oxytocin neuron ablation
562 had no significant effect on food intake in rats fed a high fat or standard diet (n=1).
563 Morris et al.[89] found PVN injection of oxytocin antisense significantly decreased salt
564 intake in baroreceptor-denervated rats, but not in healthy controls (Table 8).

565 **4. Discussion**

566 This systematic review provides a summary of preclinical studies investigating oxytocin
567 in relation to dietary intake and feeding behaviours. A total of 246 experiments in rats
568 and mice from 75 published papers were reviewed. Various oxytocin measures were
569 reported with the most common examining the effects of exogenous oxytocin
570 administration on food intake (grams, g/kg BW, mL or kcal). In addition to physical
571 dietary intake a range of feeding behaviours were also assessed. The majority of
572 studies (87%) were carried out in male rodents. While male rodents are often
573 preferred in research studies over females, due to the potential effect of hormonal
574 variations on food intake associated with the female oestrous cycle, 32 experiments
575 included female rodents. Of the thirteen experiments[9,10,15,17,49,52,53,58] that included
576 both sexes, in all but two,[49,58] exogenous oxytocin had similar effects in males and
577 females. However, two studies found females were more sensitive to lower doses of
578 oxytocin than males in reducing sucrose and food intake.[10,15] Notably, ten of the 19
579 experiments carried out exclusively in females were conducted in oxytocin KO mice.
580 This may be attributed to the tendency for male mice lacking oxytocin to develop late-
581 onset obesity.[23,94]

582 The majority of studies in this review investigated the effect of acute or chronic
583 exogenous oxytocin via central (brain delivery) or systemic administration (n=125
584 experiments). In 55% of studies, food intake or feeding behaviour was assessed over a
585 relatively short duration (<24h) and food or nutrient intake was most often reported
586 as grams consumed. Collectively the majority of studies reported a decrease in food
587 intake, sucrose and alcohol intake, in addition to decreased feeding duration and
588 increased latency to the first meal. Notably, chronic doses of oxytocin produced a
589 stronger anorexigenic effect in DIO and obese leptin resistant rodents than lean

590 controls. Acute doses of oxytocin were given up to two hours prior to feeding. For the
591 majority of studies with earlier administration times (30-120min prior to feeding)
592 oxytocin still produced positive effects on intake outcomes. This is an advantage of
593 animal studies, allowing for a more controlled environment where food intake can be
594 closely monitored, in contrast to human studies where feeding often can occur more
595 spontaneously without prompting or time to administer oxytocin. Few studies
596 reported raw data to demonstrate a reduction in food intake, but rather reported the
597 direction and quantification of the result. Results of the meta-analysis in mice and rats
598 show there was a systematic difference in the cumulative amount of food eaten in the
599 early time periods following oxytocin or vehicle administration (1-4h in rats; 1-6h in
600 mice) between oxytocin treated rodents and controls. The early decrease in food
601 intake was no longer significant 24h post-administration in either mice or rats,
602 indicative of oxytocin's declining effectiveness over time. Of the experiments included
603 in the meta-analysis, for three conducted in rats[13,15,69] and 10 conducted in mice,[37,55]
604 food was not provided immediately (within 10min) following oxytocin/vehicle
605 administration. Rats will commonly consume up to ~15-30 grams of standard chow per
606 day, and mice up to ~5-8 grams, depending on their strain and body weight.[95] Whilst
607 these numbers appear small, the oxytocin post-administration reduction in food intake
608 can be represented as a ~4-9% decrease in rats and a ~18-29% decrease in mice over
609 two hours, which contextually is a significant reduction. Importantly, not all exogenous
610 oxytocin administration experiments (n=4)[49] showed a reduction in food intake after
611 oxytocin. The reasons for these differences are not immediately apparent and
612 highlights a need to consider interactions between hormones (e.g. oxytocin +
613 cholecystokinin,[96] oxytocin + leptin[97]). Making between study comparisons difficult is

614 the tendency of preclinical studies to report only minimal information regarding
615 housing conditions which may be highly influential. Indeed, standardising housing,
616 light cycle and other laboratory conditions would make comparisons far easier. For
617 this review many of the experimental results included in the meta-analysis were
618 extracted from a graphical data using a web digitiser. The WebPlotDigitizer[27] is
619 considered accurate and has been used widely for previously published reviews,
620 however also acknowledged as a limitation of this review.[98-100] To allow for a more
621 detailed meta-analysis in the future, an important recommendation arising from this
622 review is that publications should report outcome data, including means and standard
623 deviation, and group changes in addition to the direction which was more often
624 reported.

625 Given the short half-life of oxytocin (approximately 1-6 min[101,102]) and the
626 demonstrated 1-24h reduction in food intake post-administration, exogenous oxytocin
627 may activate an indirect peripheral pathway triggering increased central release of
628 endogenous oxytocin via increased basal activity of oxytocin cells in which oxytocin
629 secretion increases. Assessing intake at regular intervals post-administration
630 throughout the experimental period, rather than a one off measure, may be beneficial
631 to address this possibility. As suggested by Leslie et al.[103] longer study durations, with
632 a regime of intermittent oxytocin administration of differing dosing schedules, are
633 needed to determine if the reduction in appetite induced by oxytocin can be
634 maintained over the longer-term (i.e. >3 weeks). This would assist in the translation to
635 human studies and enable oxytocin's effect on longer durations of habitual food intake
636 to be measured. Consideration should be given to the timing of experimental
637 protocols and data collection. Rodents, when housed under a standard 12h light/12h

638 dark cycle, will consume the majority of their daily food intake (~70%) during the dark
639 cycle, with shorter bouts of feeding during the light phase.[104] As many of the shorter
640 duration experiments (<12h) were conducted during the light phase, it is possible that
641 differences in dietary intake were not detected. Interestingly it was reported in two
642 studies[11] that the oxytocin-induced decrease in food intake was diminished when
643 animals were placed into a social context. This warrants further consideration given
644 the known role for oxytocin in social bonding and interactions in animals and humans,
645 and may suggest that the effect of oxytocin on food intake is context specific. To
646 increase the relevance of animal to human investigations, further studies observing
647 more naturalistic feeding behaviours, such as the frequency and length of meal bouts,
648 would be worthwhile. Measuring food or nutrient intake as kilojoules consumed or
649 percent of baseline intake may provide a better understanding of the interaction
650 between oxytocin and dietary intake or behaviours, making results more comparable
651 across studies.

652 The oxytocin gene deletion studies examined in our review highlight the importance of
653 oxytocin in reducing food intake, especially for highly palatable foods. This is further
654 supported by most oxytocin receptor antagonist and agonist studies. Oxytocin
655 receptor antagonists stimulated food intake by increasing meal size and feeding
656 duration. Additionally, the central (lateral ventricle, fourth ventricle and nucleus
657 accumbens core) and peripheral (IP and IV) administration of oxytocin receptor
658 antagonists blocked the hypophagic action induced by exogenous
659 oxytocin.[11,13,14,36,44,70,73-75] With the exception of two experiments,[36] oxytocin was
660 administered via the same route as the antagonist. The administration of an oxytocin
661 agonist was found to have a similar effect to oxytocin on food intake. Further studies

examining oxytocin gene expression found sucrose and sodium consumption enhanced oxytocin mRNA levels, whereas high fat diets and prolonged alcohol exposure did not change oxytocin mRNA levels. Only one of two studies found fasting as well as overfeeding led to changes in mRNA expression levels of oxytocin. Oxytocin concentrations in hypothalamic nuclei (PVN and SON) were generally unaltered by food deprivation and refeeding, with the exception of the median eminence. With respect to plasma oxytocin, the consumption of standard chow did not significantly alter plasma levels of oxytocin. Whereas, plasma levels were found to be lowered in rodents fed chow higher in fat, and elevated in those consuming liquids high in sodium. Furthermore, chronic exposure to high fat diet disrupted diurnal oxytocin release correlated with a feeding circadian pattern.

In the context of this review, very few studies investigated the effect of altered diet on endogenous oxytocin levels (n=8 endogenous studies vs. n=126 exogenous studies), in contrast to studies of oxytocin in humans. The difference may be accounted for by the fact that exogenous administration of oxytocin in humans is relatively new and more substantial ethical implications apply in human studies. Similar to the review of human studies, plasma values varied markedly across studies, consequently oxytocin concentrations cannot be compared directly between studies. A criticism that has been raised regarding the measurement of plasma oxytocin is the use of unextracted serum in enzyme immunoassay and radioimmunoassay procedures.[102,105] It has been reported that values generated for oxytocin levels in unextracted plasma can be "impossibly high and wholly erroneous measurements".[105] To resolve existing controversies further validation studies are needed, and as previously suggested, a gold-standard methodology for oxytocin measurement would be beneficial.

Within this review, the method of exogenous oxytocin administration was distinctly different to that found in human studies. Many of the included studies administered oxytocin by invasive procedures that are not possible in humans. While not directly translatable to human based studies it does provide valuable evidence of the influence of oxytocin on dietary intake. Pharmacotherapeutic drugs for the treatment of several neuropsychiatric states, including addiction and eating disorders, often require repeated administration of the prescribed drug for treatment. However, of the 126 exogenous studies reviewed here, only 25 experiments used repeated or continuous administration of oxytocin. In approximately half of these experiments (52%) study durations were ≤2 weeks. Single dose administration is less likely than repeated administrations to elicit adverse effects.[106,107] Several off-target effects have been reported in human trials (e.g. anti-social behaviours such as increased aggression,[108] decreased trust and co-operation[109]) following acute oxytocin administration. These effects are yet to be monitored following the chronic administration of oxytocin in either human or animals. Examining these effects will greatly improve understanding of the oxytocin system for future therapeutic targets. Furthermore, it is still unclear how the effects of exogenous oxytocin produces its effects on feeding behaviour. Current thinking is that exogenous (high dose) oxytocin may signal to the brain via actions at areas with porous blood brain barrier permeability (e.g. the area postrema, nucleus of the solitary tract) or actions on the vagus nerve.[8,110] Oxytocin may also act on peripheral oxytocin receptors expressed in the gastrointestinal tract.[8,111]

Limitations of the present systematic review need to be acknowledged. Firstly, the review included only published studies in English, and was limited to mice and rats. Overall samples were predominantly made up of male rodents and sample sizes were

small, potentially limiting the generalisability of the results. However, the small sample sizes may be attributable to ethical considerations to minimise animal usage. Secondly, heterogeneity (e.g. differing feeding protocols and experimental durations) among the majority of the included experiments limited the opportunity for meta-analytic synthesis of all the experiments in this systematic review. With regard to the meta-analysis, it is possible that reporting bias may have arisen due to the small sample sizes of the included studies, or potentially publication bias. Thirdly, unlike human-based studies, exact numbers of animals were often not reported or the same animals were used across experiments, potentially confounding the results. Lastly, the quality of the included articles were assessed as having an unclear risk of bias for many of the domains due to missing information. Providing detailed information regarding allocation concealment, housing, and blinding of assessors to interventions and outcomes would help improve the methodological quality of future studies. The use of ARRIVE (Animals in Research: Reporting In Vivo Experiments)[112] guidelines provide a practical resource to improve the standardisation of experimental and reporting procedures.

5. Conclusion

This review identified a large number of studies investigating the regulatory effects of oxytocin on dietary intakes in mice and rats. Exogenous studies formed the majority of included studies and it was found that the central and systemic administration of oxytocin significantly reduced food intakes in both lean and obese rodents. The greatest effects on food intake were observed in the short term, 1h post-

administration. The underlying neural mechanisms with respect to the behavioural aspects of diet and eating warrant further investigation.

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Declaration of interest

The authors have no relevant interests to declare.

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Supplementary Material

Table S1. PRISMA-P 2015 Checklist for studies included in the systematic review

Table S2. Search Strategy (April 2018)

Table S3. Database search: MEDLINE 1970 to Present

Table S4. Database search: Embase Classic + Embase 1970 to 2018 April 5

Table S5. Database search: CINAHL 1998 - 2018

Table S6. Database search: COCHRANE 1970 – 2018 April 5

Table S7. Database search: Scopus 1970 – 2018 April 5

752 Table S8. Database search: Scopus 1970 – 2018 April 5

753 Table S9. Study Quality and Risk of Bias assessment

754 Table S10. Descriptions and outcomes of studies included in meta-analysis: effect of
755 acute exogenous oxytocin administration on food intake in rats

756 Table S11. Descriptions and outcomes of studies included in meta-analysis: effect of
757 acute exogenous oxytocin administration on food intake in mice

758 R Code for Meta-analysis: Effect of acute exogenous oxytocin administration on food
759 intake in rats

760 R Code for Meta-analysis: Effect of acute exogenous oxytocin administration on food
761 intake in mice

762 Figure S1. Forest plot for meta-analysis of effect of acute exogenous oxytocin
763 administration on food intake in rats S1. Forest plot for meta-analysis of effect of
764 acute exogenous oxytocin administration on food intake in rats

765 Figure S2. Funnel plot for a meta-analysis of effect of acute exogenous oxytocin
766 administration on food intake in rats

767 Figure S3. Residual plot for a meta-analysis of effect of acute exogenous oxytocin
768 administration on food intake in rats

769 Figure S4. Forest plot for meta-analysis of effect of acute exogenous oxytocin
770 administration on food intake in mice

771 Figure S2. Funnel plot for a meta-analysis of effect of acute exogenous oxytocin
772 administration on food intake in mice

Figure S3. Residual plot for a meta-analysis of effect of acute exogenous oxytocin administration on food intake in mice

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Table 1. Descriptions and outcomes of included exogenous oxytocin studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Altirriba et al. (2014)[33] *Switzerland*	Food intake	Mice C57BL/6JRj (lean) and B6.V-Lepob/JRj^ (ob/ob) ^ model of obesity, hyperinsulinemia & diabetes	22-38 ob/ob, 13-19 lean	M	8 wk	14 d	NR	SC infusion via 14d osmotic pump: OT 5 and 50nmol/day vs. OT analogue with higher OT receptor specificity (TGOT = [Thr4,Gly7]-OT) 50nmol/day vs. saline	Food intake (standard chow) measured daily (grams)	OT 50nmol/day vs. saline: in ob/ob mice significantly reduced food intake on days 1-7, 10, 13-14 ($p<0.05$), effects more marked during 1st week; in lean mice significant effect on day 1 only ($p<0.001$), days 2-14 $p=0.07$. OT 5nmol/day vs. saline, and TGOT 50nmol/day vs. saline: in ob/ob mice no effect on food intake ($p>0.05$).	↓ in ob/ob (OT 50nmol)
Arletti et al. (1989)[13] *Italy* Experiment 1	Food intake	Rat Sprague-Dawley	108 (27/group)	M	NR	3 h	Natural light-dark cycle	4 test conditions: 1) LV OT 1µg/rat vs. 2) LV OT 2µg/rat vs. 3) LV OT 10µg/rat vs. 4) LV saline; injected 5min before feeding.	Cumulative food intake (standard chow) measured hourly (grams) following 21h fast	OT decreased food intake, one hr: $F(3,104)=17.78$, $p<0.0001$; 2 hr: $F(3,104)=13.73$, $p<0.0001$; 3hr: $F(3,104)=5.27$, $p<0.0006$.[a] Lower doses of OT (1 and 2µg/rat) significantly reduced food consumption only during first hour ($p<0.05$). Highest dose (10µg/rat) significantly reduced food intake for 3 h ($p<0.05$).	↓
Arletti et al. (1990)[14] *Italy* Experiment 2	Food intake	Rat Sprague-Dawley	32 (≥10 per group)	M	NR	1 h	Natural light-dark cycle	4 test conditions: 1) LV OT 1µg/rat vs. 2) LV OT 10µg/rat vs. 3) LV saline; 4) IP OT 375µg/kg. Injected just before feeding.	Food intake (standard chow) measured (g/hour), latency to 1st meal, meal duration and no. of meals.	ICV OT significantly reduced food intake at dose of 1 µg/rat ($p<0.05$), and completely inhibited food intake at dose of 10 µg/rat ($p<0.001$).[a]	↓

Arletti et al. (1990)[14] *Italy* Experiment 3	Food intake	Rat Sprague-Dawley	56 (≥10 per group)	M	NR	1 h	Natural light-dark cycle	4 test conditions: 1) IP OT 750µg/kg vs. 2) IP OT 1500µg/kg vs. 3) IP OT 3000µg/kg vs. 4) IP saline. Injected just before feeding.	Food intake (standard chow) measured (g/hour), latency to 1st meal, meal duration and no. of meals.	IP OT significantly reduced food intake [F(3,41)= 11.15, p<0.0001].[a] Doses of 375, 750 and 1500 µg/kg (p<0.01); 3000 µg/kg almost complete inhibition of food intake (p<0.001).[a] [Researchers note doses lower than these were ineffective].	↓
Balazova et al. (2016)[59] *Slovakia*	Food intake	Rats Zucker	7 treatment (lean) 7 vehicle (lean) 7 treatment (obese, leptin-resistant) 7 vehicle (obese, leptin-resistant)	M	10 weeks	2 weeks	12h light/ 12h dark	SC OT infusion via mini pump: 3.6 µg/100 g BW/day vs. saline. Plasma OT measured by EIA.	Standard chow diet and water available ad lib. Food intake measured daily (g/day).	Presence of hyperphagia (F(1,24) = 34.88; p < 0.001).[a] Significant main effect of treatment on cumulative 2 week food intake (F(1,24)=8.35; p<0.01) and daily food intake (F(1,24)=8.29; p<0.01) in obese and lean rats.[a] Exogenous OT resulted >6-fold increase in plasma OT [F(1,24)=27.01; p<0.001].	↓
Benelli et al. (1991)[15] *Italy* Experiment 1	Food intake	Rats Wistar	≥10/group	M & F	Adult	1 h	Natural light-dark cycle	3 test conditions: 1) LV OT 1µg/rat vs. 2) LV OT 10µg/rat vs. 3) LV saline; injected just before feeding.	Standard chow diet and water available ad lib. Male and female food intake measured (g/hour) following 21 h fast.	Dose of 1µg/rat OT decreased food intake by ~50% (p<0.05), feeding completely abolished at dose 10µg/kg (p<0.001) in males and females.[a]	↓
Benelli et al. (1991)[15] *Italy* Experiment 2	Food intake	Rats Wistar	≥10/group	M & F	Adult	1 h	Natural light-dark cycle	4 test conditions: 1) IP OT 187µl/kg vs. 2) IP OT 375µl/kg vs. 3) IP OT 750 µl/kg vs. 4) IP saline; injected just before feeding	Standard chow diet and water available ad lib. Male and female food intake measured (g/hour) following 21 h fast..	Males: OT decreased food intake at doses 187 and 375µg/kg by ~30% (p<0.05), 750µg/kg by ~60% (p<0.01); Females: OT decreased food intake at dose 187 by ~30% (p<0.05), doses of 375 and 750µg/kg by ~60% (p<0.01) [interrupted from graph].[a]	↓

Bernal et al. (2007)[65] *Spain* Experiment 1	Food intake	Rats Wistar	8 treatment 8 vehicle	M	Adult	3 d	12h light/ 12h dark (lights on 0800)	SC 0.5mL OT 10IU/mL vs. saline; 2x injections on injected on day-2 at 0830 and 1430 h.	24 h baseline period. During following 48 h, food and water available ad lib. 3 x 24 h food intake recorded (g/day).	No significant differences in food intake between OT and control groups on any day (data not shown).	↔
Bernal et al. (2010a)[66] *Spain*	Food intake	Rats Wistar	7 treatment 7 vehicle	M	Adult	3 d	12h light/ 12h dark (lights on 0800)	SC 0.5mL OT 11µg vs. vehicle (distilled water); 2x injections on day-3 at 0830 and 1430 h.	48 h pre-injection period (2nd 24 h = baseline period, food intake measured g/day). During following 24 h, food and water available ad lib. 12 h food intake recorded (g/12 hours) on day 3 (0830-2030 h).	Food intake – Baseline 24h food intake (g): vehicle= 25±1, OT= 25±1; Treatment day 12h food intake (g): vehicle= 7.4±0.9, OT= 5.5±0.7.[b] No significant differences in food intake before or after OT administration.	↔
Bernal et al. (2010b)[67] *Spain*	Food intake	Rats Wistar	40 treatment 40 vehicle	M	Adult	3 d	12h light/ 12h dark (lights on 0800)	SC 0.5mL OT 22µg vs. vehicle (distilled water); injected on day 3 at 0830 and 1430 h.	48 h pre-injection period (2nd 24 h = baseline period, food intake measured g/day). During following 24 h, food and water available ad lib. 12 h food intake recorded (g/12 hours) on day 3 (0830-2030 h).	Food intake – Baseline 24h food intake (g): vehicle= 24.8±0.3, OT= 24.8±0.4; Treatment day 12h food intake: vehicle= 7.95±0.37, OT= 6.67±0.61.[b] No differences in food intake 1st 72 h between groups. Non-significant reduction in food intake following OT administration.	↔
Bjorkstrand et al. (1996)[49] *Sweden* Experiment 1	Food intake	Rat Sprague-Dawley	19 (9 F, 10 M)	M & F	M=6 wk F=8 wk	72 h, 1 week interval between injections	12h dark/ 12h light (light on 2200)	One dose LV OT 5µg/rat vs. LV saline, crossover design. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day). Water and food available ad lib.	Female food intake (g) – 0-24 h: OT = ~19, saline = ~17; 24-48 h: OT = ~21, saline = ~21; 48-72 h: OT = ~21, saline = ~22. Male food intake (g) – 0-24 h: OT = ~23, saline = ~22; 24-48 h: OT = ~25, saline = ~28; 48-72 h: OT = ~28, saline = ~31 [Interpreted from graph]. OT-treated females ate significantly more during first 24 h period ($p < 0.01$).[a] In males no difference between OT and saline treatment.[a]	↑ females (0-24 h), ↔ males

Bjorkstrand et al. (1996)[49] *Sweden* Experiment 2	Food intake	Rat Sprague-Dawley-	8	F	8 wk	3 d	12h dark/ 12h light (light on 2200)	Once a day LV OT 5µg/rat vs. LV saline, crossover design. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day). Water and food available ad lib.	First 24 h, OT-treated ate more food than saline-treated, 21±6 vs 14±5g (NS).[b] Entire 72 h period, OT-treated ate significantly more than saline-treated, 18±4 vs 13±5 g/day ($p < 0.05$).[b]	↑
Bjorkstrand et al. (1996)[49] *Sweden* Experiment 3	Food intake	Rat Sprague-Dawley	5 treatment 5 vehicle	F	8 wk	72 h	12h dark/ 12h light (light on 2200)	One dose LV OT 5µg/rat vs. LV saline. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day) following 24 h food deprivation. Water and food available ad lib.	Entire 72 h period, OT-treated ate significantly more than saline-treated, 26±6 vs 18±2g/day ($p < 0.05$).[b]	↑
Bjorkstrand et al. (1996)[49] *Sweden* Experiment 4	Food intake	Rat Sprague-Dawley	25 treatment (4,11 and 10/group) 25 control	F	8 wk	24 h	12h dark/ 12h light (light on 2200)	4 test conditions: 1) LV OT 1µg/rat vs. 2) LV OT 5µg/rat vs. 3) LV OT 10µg/rat vs. 4) LV saline. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day). Water and food available ad lib.	OT 1 µg = no affect (data not shown). Dose-related effect seen for 5µg and 10µg; OT-treated ate significantly more than saline-treated (5µg dose= 24±2 vs 21±2g, $p<0.05$; 10µg dose= 20±4 vs 18±2g, NS).[b]	↑
Bjorkstrand et al. (1996)[49] *Sweden* Experiment 5	Food intake	Rat Sprague-Dawley	6	F	8 wk	72 h, 1 week interval between injections	12h dark/ 12h light (light on 2200)	One dose IP OT 5µg/rat vs. ICV saline, crossover design. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day). Water and food available ad lib.	24h food intake (g): OT= 24+5, saline= 21+3. 48[b]; (48h and 72h data not shown). IP OT had no effect on 24, 48 or 72 h food intake.	↔
Bjorkstrand et al. (1996)[49] *Sweden* Experiment 6	Food intake	Rat Sprague-Dawley-Strain B^ ^ Rapidly growing model with high plasma OT, CCK, & insulin; low plasma somatostatin	6 treatment 6 vehicle	M & F	M=6 wk F=8 wk	24 h	12h dark/ 12h light (light on 2200)	One dose LV OT 5µg/rat vs. LV saline. Injected at start of dark phase.	Food intake (standard chow, protein content 18.5% for females and 16.5% for males) measured (g/day). Water and food available ad lib.	ICV OT had no effect on 24 h food intake (data not shown).	↔

Blevins et al. (2016)[16] *USA* Experiment 1	Food intake	Rat Sprague-Dawley SD-SAS	7-9/group DIO (treatment and vehicle)	M	~2.5-6 mo	3 d	12h light/ 12h dark (lights on at 1300)	SC OT infusion via 14 d mini pump of varying doses: 50nmol/day vs. 100nmol/day vs. 200nmol/day vs. saline	Daily food intake (standard chow) recorded (kcal/day). Food available ad lib.	Effect on food intake unclear at low doses. OT reduced energy intake on day 2 at 50 (p=0.055), 100 (p=0.1), and 200 nmol/day (p=0.092).[a]	↔
Blevins et al. (2016)[16] *USA* Experiment 2	Food intake	Rat Sprague-Dawley CD® IGS*	3-5/group (post-treatment and post-vehicle)	M	~2.5-6 mo	28 d	12h light/ 12h dark (lights on at 1300)	Effects of treatment cessation i.e. no OT infusion (mini pump removed from experimental DIO rats after 38 days OT treatment)	Daily food intake recorded (kcal/day) in 3 h fasted rats.	No significant difference in food intake between post-oxytocin vs. post-vehicle groups.[a]	↔
Diaz-Cabiale et al. (2000)[68] *Sweden*	Food intake	Rat Sprague-Dawley	8 satiated	M	NR	22h, 48 h interval between injections	14h light/ 8h dark (lights on 0600)	LV OT 1nmol vs. saline, crossover design; injected 60min before feeding.	Food intake (standard chow) measured (grams) 30, 90, 4 h and 22 h. Testing 1 h after satiation (i.e. mice fed standard pellets dipped in milk).	OT had no effect on food intake in satiated mice; slight non-significant increase in feeding response at 240min (p>0.05).[a]	↔
Herisson et al. (2016)[11] *NZ* Experiment 1	Food intake	Rats Sprague-Dawley	8-9/group treatment 8 vehicle	M	Adult	24 h	12h light/ 12h dark (lights on 0700)	Intracranial (nucleus accumbens core or shell) OT 0.3, 1 and 3µg vs. saline; injected 5min before feeding (1000 h).	Food intake (standard chow) measured (grams) at 2, 4 and 24 h following overnight food deprivation. Rats were deprived of chow overnight. Water available ad lib.	Core, but not shell injections of OT affected food intake. 1 and 3µg OT in AcbC decreased food intake by ~35–40% at 2 h (1µg, p=0.028; 3µg, P = 0.019) and 4 h (1µg, p=0.006; 3µg, p=0.004).[a] No effect at 24 h (data not shown).	↓
Ho et al. (2014)[36] *USA* Experiment 1	Food intake	Rats Sprague-Dawley	12/group	M	Adult	18 h	12h dark/ 12 h light (lights on 0100)	2 injections spaced 30min apart: 1) IP vehicle (saline) and 2) IP vehicle or OT (0.5 mg/kg), crossover design. 2nd injection given 10 min before feeding.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at intervals for 18 h.	Food intake significantly reduced at 30min only (t11=3.284, p=0.007).[a]	↓
Ibragimov et al. (1988)[69] *Hungary* Experiment 1	Food intake	Rats CFY albino	10/group	M	NR	30min	12h light/ 12h dark (lights on 0600)	IP OT 300, 600 and 1200mU/kg vs. saline; injection 20min before feeding.	Food intake (standard chow; g/30 min) following 22 h food deprivation.	Food intake (g): Saline = 3.37±0.30, OT 300 mU/kg = 3.30± 0.38, OT 600 mU/kg = 3.16±0.39, OT 1200 mU/kg = 3.45±0.27.[b] No significant difference between groups.	↔

Iwasaki et al. (2014)[50] *Japan* Experiment 1	Food intake	Mice C57BL/6J	8/group	M	8-12 wk	6 h	12h light/ 12h dark (lights on 0730)	IP OT 200 and 400µg/kg vs. saline; injection 10min before feeding (dark cycle).	Standard chow provided at 1930, following 2 h fast. Cumulative food intake recorded (grams).	OT 200 and 400µg/kg significantly reduced food intake vs. vehicle 0.5-6 h ($p<0.01$).[a] Greater reduction with OT dose 400µg/kg vs. 200µg/kg for 0.5-3 h ($p<0.05$).[a]	↓
Iwasaki et al. (2014)[50] *Japan* Experiment 2	Food intake	Mice C57BL/6J	6/group	M	8-12 wk	6 h	12h light/ 12h dark (lights on 0730)	IP OT 200µg/kg vs. saline; injection 10min before feeding (dark cycle).	Liquid-diet (human infant formula) provided at 1000, following overnight fast (16 h). Cumulative liqid-diet intake recorded (grams).	OT significantly reduced liquid-diet intake vs. vehicle at 0.5 and 1 h ($p<0.01$), NS reduction from 1-6 h.[a]	↓
Iwasaki et al. (2014)[50] *Japan* Experiment **3**	Food intake	Mice C57BLKS/J (BKS) db/db	6 treatment 6 vehicle	M	9-12 wk	a) 6 h	12h light/ 12h dark (lights on 0730)	Single IP OT 200µg/kg vs. saline; injected before feeding (dark cycle).	Hourly (cumulative) food intake (standard chow) measured (g).	OT significantly reduced food intake vs. vehicle for 0.5-3 h ($p<0.01$); NS difference at 6 h.[a]	↓
Iwasaki et al. (2014)[50] *Japan* Experiment 4	Food intake	Mice C57BLKS/J (BKS) db/db	10 treatment 7 vehicle	M	9-12 wk	12 d	12h light/ 12h dark (lights on 0730)	SC OT via mini pump: 1600µg/kg/day vs. saline	Daily (g/day) and cumulative food intake (standard chow) measured.	OT significantly reduced daily food intake vs. vehicle from day 2-12 (days 2 and 6, $p<0.05$; days 8-12, $p<0.01$) cumulative food intake for 12 days ($p<0.01$).[a]	↓
Klockars et al. (2017a)[73] NZ & USA Experiment 1	Food intake	Rats Sprague-Dawley	8-9/group all food-deprived	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.03, 0.1, and 0.3µg/kg vs saline; injection prior to refeeding.	Following overnight food deprivation, food intake (standard chow, 3.6kcal/g) measured (grams) 1 h and 2 h post-injection. Water available ad lib.	ICV OT lowered deprivation-induced food intake 1 and 2h at dose of 0.1µg/kg (1 h: $p=0.0495$, 2 h: $p=0.0141$), and 0. µg/kg (1h: $p=0.0187$, 2 h: $p=0.0130$); decrease was similar for both doses.	↓
Klockars et al. (2017b)[75] NZ & USA Experiment 1	Food intake	Rats Sprague-Dawley	6-7/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VMH OT 0.3µg vs. OT 1.0µg vs. saline; injected just before testing.	Following overnight food deprivation, food intake (standard chow) measured (grams) 1 h and 2 h post-injection.	VMH OT significantly decreased deprivation-induced food intake at 1 h (1.0µg, $p=0.0027$) and 2 h (0.3µg, $p=0.0324$; 1.0 µg, $p=0.003$) post-injection.	↓

Klockars et al. (2017b)[75] NZ & USA Experiment 4	Food intake	Rats Sprague-Dawley	7/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VMH OT 0.3µg vs. OT 1.0µg vs. saline; injected just before testing.	Food intake (standard chow) of once a day (2 h access) schedule fed rats measured (grams) 1 h and 2 h post-injection.	VMH OT 1.0µg significantly reduced consumption at 2h (p=0.0014), no significant reduction at 1h for doses 0.3 and 1.0µg.	↓ (1.0µg at 2 h)
Klockars et al. (2018)[74] NZ & USA Experiment 1	Food intake	Rats Sprague-Dawley	11/group	M	Adult	24h	12h light/ 12h dark cycle (lights on 0700)	BLA OT 0.1, 0.3 and 1.0µg vs. saline; injected just before testing.	Following overnight food deprivation, food intake (standard chow) measured (grams) 2 h, 4 h and 24 h post-injection.	BLA OT 0.3 and 1.0µg significantly decreased food intake after 2 h [F(3, 30)=5.575, p=0.0012 and p=0.022, respectively] and 4 h post-injection [F(3, 30)=4.73; p=0.011 and p=0.046, respectively]. No differences at 24 h.	↓ (0.3 and 1.0µg)
Klockars et al. (2018)[74] NZ & USA Experiment 2	Food intake	Rats Sprague-Dawley	10/group	M	Adult	24h	12h light/ 12h dark cycle (lights on 0700)	CNA OT 0.1, 0.3 and 1.0µg vs. saline; injected just before testing.	Following overnight food deprivation, food intake (standard chow) measured (grams) 2h, 4h and 24 h post-injection.	CNA OT 1µg significantly reduced food intake at 2h [F(3, 27)=5.41, p=0.0042], and 4h [F(3, 27)=3.787, p=0.015]. No differences at 24 h.	↓ (1.0µg)
Maejima et al. (2011)[55] Japan Experiment 1	Food intake	Mice C57BL/6J	5/group DIO	M	6 wk	24 h	12h light/ 12h dark cycle (lights on 0700)	IP OT 200µg/kg vs 400µg/kg vs. vehicle (saline); injected immediately prior to feeding (start of dark phase).	Cumulative food intake (grams) 0.5, 1, 2, 3, 6 and 24 h measured. Food (standard chow) and water available ad lib.	IP OT 200 ($p<0.05$) and 400µg/kg ($p<0.01$) significantly suppressed cumulative food intake for 0.5 to 6 h, compared to vehicle.	↓ (0.5 to 6 h)
Maejima et al. (2011)[55] Japan Experiment 2	Food intake	Mice C57BL/6J	5/group DIO	F	6 wk	24 h	12h light/ 12h dark cycle (lights on 0700)	SC OT 1,600µg/kg vs. vehicle (saline); injected 2 h prior to feeding (start of dark phase).	Cumulative food intake (grams) 1, 2, 3, 6 and 24 h measured. Food (standard chow) and water available ad lib.	SC OT 1,600µg/kg significantly suppressed cumulative food intake for 1 to 6 h, compared to vehicle ($p<0.01$).	↓ (0.5 to 6h)
Maejima et al. (2014)[51] *Japan* Experiment 1	Food intake	Rats Wistar	10 treatment 10 vehicle	M	Adult	24 h	12h light/ 12h dark (lights on 0730)	LV injection of OT 4nmol/5µl vs saline, given just before onset of dark phase and feeding.	Cumulative food intake (grams) 1, 3, and 6 h measured; 3 h food deprivation prior to testing. Food (standard chow) and water available ad lib.	LV OT significantly reduced cumulative [$F_{1,36}=63.24$, $p<0.01$] and periodical food intake [$F_{1,36} = 4.11$, $p<0.01$].[a] Periodical food intake: 0–1 h, 1–3 h and 3–12 h in OT	↓

										group was 38% (p<0.01), 110% and 77% (p<0.05) of that in vehicle group.[a]	
Maejima et al. (2014)[51] *Japan* Experiment 2	Food intake	Rats Wistar	8 treatment 8 vehicle	M	Adult	24 h	12h light/ 12h dark (lights on 0730)	Intra-ARC injection OT 0.4 nmol/0.5µl vs saline, given just before onset of dark phase and feeding.	Cumulative food intake (grams) 1, 2, 3, 12 and 24 h measured; 3 h food deprivation prior to testing. Food (standard chow) and water available ad lib.	Intra-ARC injection of OT significantly reduced cumulative food intake at 1 and 12 h after injection [F1,56 = 18.47, p<0.01].[a] Periodical food intake: 0–1 h, 1–2 h, 2–3 h, 3–12 h and 12–24 h in OT group was 50%, 145%, 85%, 95% and 187% of that in vehicle group (NS in all time periods).[a]	↓
Maejima et al. (2015)[37] *Japan* Experiment 1	Food intake	Mice C57BL/6J	8-13/group	M	6 wk	24 h	12h light/ 12h dark (lights on 0730)	Nasal OT 0.1–10 µg/10 µl	Cumulative food intake for 0.5, 1, 2, 6, and 24 h measured. 2 h food deprivation prior to testing. Food (standard chow) and water available ad lib.	Nasal OT: 0.1µg no significant effect on food intake [F1,60=2.53, p>0.05]; 1µg significantly decreased food intake [F 1,56 = 27.4, p<0.01], and 10µg [F1,92=27.16, p<0.01].[a] Nasal 1µg OT reduced cumulative food intake 6 and 24 h (p<0.01), and 10µg at 0.5, 1, 2, 6, and 24 h (p<0.01).	↓
Maejima et al. (2015)[37] *Japan* Experiment 2	Food intake	Mice C57BL/6J	12 (4/group)	M	6 wk	24 h	12h light/ 12h dark (lights on 0730)	IP OT 40 and 400 µg/kg vs saline; given 30min before dark phase and feeding.	Cumulative food intake for 0.5, 1, 2, 6, and 24 h measured. 2 h food deprivation prior to testing. Food (standard chow) and water available ad lib.	IP OT: 40µg/kg no significant effect on food intake [F1,24=2.27, p > 0.05] and 400 µg/kg significantly decreased food intake at 0.5, 1, 2, and 6 h [F1,24=38.9, p<0.01] but not at 24 h.[a]	↓
Maejima et al. (2017)[58] Japan Experiment 3	Food intake	Mice C57BL/6J	19 control 19 treatment	M	14 wk (M) 18 wk (F)	10 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 800 or 1,600 µg/kg/day vs. saline [specific OT dose not reported].	Mice maintained on standard diet; 24 h food intake measured (grams) everyday at 17:00 (2 h before onset of dark phase).	OT significantly decreased food intake on day 2 only [(F1,126)=6.56, p<0.05].	↔

Maejima et al. (2017)[58] Japan Experiment 4	Food intake	Mice C57BL/6J	19 control 20 treatment	F	14 wk (M) 18 wk (F)	10 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 800 or 1,600 µg/kg/day vs. saline [specific OT dose not reported].	Mice maintained on standard diet; 24 h food intake measured (grams) everyday at 17:00 (2 h before onset of dark phase).	OT significantly decreased food intake on day 10 only [(F1,117) = 5.03, p<0.05].	↔
Morton et al. (2012)[38] *USA* Experiment 1	Food intake	Rats Sprague-Dawley	19/group DIO (leptin resistant-acquired) 20/group lean	M	Adult	18 h	12h light/ 12h dark	IP OT 125, 250, 500 or 1,000µg/kg LBM or saline (crossover design); injected just before feeding.	Rats maintained on either HFD (DIO) or LFD (lean). Food available ad lib from onset of dark cycle, intake measured (grams) at 4 h and 18h.	DIO and lean rats: OT reduced 4 h food intake vs. vehicle (p<0.05).[a] At 18 h, 500 and 1000µg/kg LBM significantly reduced intake (p<0.05).[a]	↓ at 4 h (all doses) ↓ at 18 h (500 and 1000µg/kg)
Morton et al. (2012)[38] *USA* Experiment 2	Food intake	Rats Koletsky (leptin receptor-deficient-genetic)	6 obese 6 lean	M	Adult	18 h	12h light/ 12h dark	IP OT 1,000µg/kg LBM or saline (crossover design); injected just before feeding.	Food available ad lib from onset of dark cycle (6 h fast prior), intake measured (grams) at 4 h and 18h	Obese rats: OT vs vehicle reduced food intake at 4 h (↓ 35%) and 18 h (↓19%), p<0.05.[a] Lean rats: OT vs. vehicle reduced food intake at 4 h and 18 h (NS).[a]	↓ (obese only)
Morton et al. (2012)[38] *USA* Experiment 3	Food intake	Rats Sprague-Dawley	5-8/group DIO 13 lean	M	Adult	18 h	12h light/ 12h dark	3V ICV 1µg or saline; injected just before feeding.	Rats maintained on either HFD (DIO) or LFD (lean). Food available ad lib from onset of dark cycle, intake measured (grams) at 4 h and 18h	DIO and lean: OT vs. vehicle significantly reduced food intake at 4 h and 18 h, p<0.05.[a]	↓
Morton et al. (2012)[38] *USA* Experiment 4	Food intake	Rats Sprague-Dawley	8/group DIO	M	Adult	7 d	12h light/ 12h dark	Daily IP OT 1,000µg/kg LBM vs. saline; injected just before feeding.	Rats maintained on HFD. Food available ad lib from onset of dark cycle, intake measured (kcal/day) at 4 h and 18h	OT vs. vehicle significantly reduced daily food intake (5 out of 7 days).[a]	↓
Noble et al. (2014)[46] *USA* Experiment 1	Food intake	Rats Sprague-Dawley	12 naïve	M	Adult	24 h	12h light/ 12h dark (lights on 0400)	Bilateral VMH (per side) OT 0.1nmol or OT 0.5nmol or OT 1.0nmol or vehicle (aCSF), crossover design; injected 30 min before feeding.	After 1 h fast, food (standard chow) available ad lib at onset dark cycle, intake measured (grams) at 1, 2, 3 and 4 h; and cumulative intake 24 h post-injection.	Food intake (g) at 1 h[b]: Control = 3.7±0.7, OT 0.5nmol = 1.8±0.5, OT 1.0nmol = 1.3±0.4, data for OT 0.1nmol dose graphed.[a] Food intake (g) at 4 h[b]: Control = 9.8±1.2, OT 0.1nmol = 7.0±1.1, OT 0.5nmol = 6.4±1.0, OT 1.0nmol = 7.6±0.8. Food intake (g) at 24 h[b]: Control = 24.7±1.3, OT 0.1nmol =	↓ (up to 4 h)

										23.8±1.1, OT 0.5nmol = 25.4±1.6, OT 1.0nmol = 23.8±1.1. During 1st hour OT vs. vehicle significantly reduced food intake by 52% (0.5nmol) and 66% (1.0nmol), p<0.05. After 4 h, OT vs. vehicle significantly reduced feeding: 0.1nmol by 27%, 0.5nmol by 34% and 1nmol by 22%, all p<0.05. Cumulative intake at 24 h not different between groups (p=0.4).	
Noble et al. (2014)[46] *USA* Experiment 2	Food intake	Rats Sprague-Dawley	12 naïve	M	Adult	4 h	12h light/ 12h dark (lights on 0400)	Bilateral VMH (per side) OT 0.1nmol or OT 1.0nmol or vehicle (aCSF), crossover design; injected 3 h into light cycle, just before feeding .	After 16 h fast, food (standard chow) available ad lib, intake measured (grams) at 1, 2, and 4 h	Food intake (g) at 1 h[b]: Control = 5.0±0.9, OT 0.1nmol = 3.6±0.5, OT 1.0nmol = 2.5±0.3. Food intake at 2 h graphed.[a] Food intake (g) at 4 h[b]: Control = 9.3±0.8, OT 0.1nmol = 7.8±0.7, OT 1.0nmol = 7.6±0.5. Food intake (g) at 24 h[b]: Control = 30.0±1.6, OT 0.1nmol = 27.7±1.5, OT 1.0nmol = 27.5±1.5. During 1st hour OT vs. vehicle significantly reduced food intake by 38% (0.1nmol) and 56% (1.0nmol), p<0.05. By 4 h, both OT groups vs. vehicle had cumulative reduction in feeding by 18%, p<0.05. After 24 h, food intake not different between groups (p=0.2).	↓ (up to 4 h)
Noble et al. (2014)[46] *USA* Experiment 3	Food intake	Rats Sprague-Dawley	8	M	Adult	12 h	12h light/ 12h dark (lights on 0400)	Unilateral VMH OT 1.0nmol or vehicle (aCSF), crossover design; injected 30 min before start of dark cycle	After 1.5 h fast, food (standard chow) available ad lib at onset dark cycle, intake measured (grams) at 12 h	12-h cumulative intake of OT group significantly less than vehicle-treated controls (p<0.05).[a]	↓

Olson et al. (1991a)[70] *USA* Experiment 1	Food intake	Rats Sprague-Dawley	3 (0.5nmol dose) 8 (1nmol dose) 8 (2nmol dose) 8 (4nmol dose)	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	LV OT 0.5nmol or OT 1.0nmol or OT 2.0nmol or OT 4.0nmol vs. vehicle (aCSF), within subject design; injected just before morning feeding.	Food intake (standard chow) measured (grams) following 16 h fast	Baseline food intake: 9.0±0.8g.[b] OT significantly decreased food intake at doses of 0.5, 1, 2 and 4 nmol [F(4,29)=7.34, p<0.001]; 1.0nmol OT vs. saline, p<0.05; 2.0nmol OT vs. saline, p<0.01; 4.0nmol vs. saline, p<0.001.[b]	↓
Uvnas-Moberg et al. (1996)[62] *Sweden* Experiment 1	Food intake	Rats Sprague-Dawley (RGR, rapidly growing rats)	18/group	F	10 wk	4 d	12h light/ 12h dark (lights on 0600)	Daily SC 1.0mg/kg OT vs. vehicle (saline); injected at 1800 (onset of dark period when rats feed). Baseline plasma OT measured via RIA =64.3±11.8 pmol/L (significantly higher level than in SGR rats in exp. 2, p<0.01).	Ad lib access to food (standard chow) and water, intake measured daily (g/4-days).	OT vs. vehicle significant decrease in food intake (p<0.001).[a]	↓
Verty et al. (2004)[63] *Australia*	Food intake	Rats Wistar	8	M	8-10 wk	120 min	12h dark/ 12h light, (lights off 0800)	LV OT 0.1, 1.0 or 10.0IU vs. vehicle (saline), within subject design; injected just before feeding at 0830 h	Ad lib access to food (standard chow) and water; intake measured (grams) at 60 and 120 min.	OT vs. vehicle decreased food intake with significant main effect of dose [F(3,21)=23.24, p<0.001].[a] OT doses 1.0 and 10.0 IU significantly different from vehicle.[a] OT 10 IU dose significantly different from 0.1 and 1.0 IU doses.[a] Significantly more food consumed in first hour relative to second hour [F(1,7)=22:85, p<0.01].[a] Dose x bin (1st or 2nd hour) interaction NS.	↓ (OT 1.0 and 10.0IU)
Zhang et al. (2011)[45] *USA* Experiment 1	Food intake	Mice C57BL/6	5-6/group, DIO	M	Adult	1 wk	12h light/ 12h dark	Daily 3V injection: 1) 1µg OT start of daytime and vehicle (aCSF) at start of nighttime, vs. 2) 1µg OT start of nighttime and vehicle at start of daytime, vs. 3) vehicle at start of daytime and nighttime	Ad lib access to food (HFD). Food intake and diurnal ratio (daytime caloric intake divided by nighttime caloric intake) measured (kcal).	OT (day and nighttime injections) vs. saline significantly decreased food intake (p<0.05). Diurnal ratio (daytime:night-time feeding) decreased by daytime OT and increased by nighttime OT treatment.	↓ food intake ↓ diurnal ratio (AM OT admin.) ↑ diurnal ratio (PM OT admin.)

Zhang et al. (2011)[45] *USA* Experiment 2	Food intake	Mice C57BL/6	5-8/group, DIO	M	Adult	6 wk	12h light/ 12h dark	Daily IP 1mg/kg OT vs. saline injected start of daytime	Ad lib access to HFD. Weekly daytime (AM), nighttime (PM) and total food intake, and diurnal ratio (daytime caloric intake divided by nighttime caloric intake) measured (kcal).	OT vs. saline significantly reduced daytime food intake ($p<0.05$), but not nighttime. OT vs. saline normalised diurnal ratio (daytime:night-time feeding).	↓ AM intake ↔ PM intake ↑ diurnal ratio
Lokrantz et al. (1997)[64] *Sweden* Experiment 1	Glucose intake	Rats Sprague-Dawley	8 naïve, food deprived	M	NR	IO glucose infusion until satiety criterion met	12h light/ 12h dark	LV OT 5nmol vs. 10nmol vs. 20 nmol vs. saline (crossover design); injected before intake test (2x test) during light phase.	12.5% glucose (wv) delivered intraorally via peristaltic pump rate of 1.0 ml/min. Total intake measured (mL). 20 h food deprivation prior to testing.	First-test intake: decline in glucose intake with increasing OT dose [$F(3,21)=10.43$, $p<0.0002$].[a] OT doses 10 nmol ($p<0.02$) and 20 nmol ($p<0.0001$) vs. saline decreased intakes significantly.[a] Second-test intake: increased intake with increasing OT dose.[a] As a result, total session intakes were unchanged by any OT treatment.	↔
King et al. (2017)[12] *USA* Experiment 8	Sucrose intake	Mice C57BL/6J	18	M	9-10 wk	20min sessions	Reversed 12h light/ 12 h dark cycle	IP OT 0.1, 0.3 and 1.0mg/kg vs. saline, crossover design; injections 30min prior to testing.	Operant self-administered by 2 lever press (active/inactive): 5% sucrose solution intake (mL/kg) measured. Stable response rates on fixed- ratio-4 schedule established prior to testing.	Marginal OT dose effect on active lever responding, [$F(3, 51) = 2.48$; $p<0.07$], and a significant effect on ml/kg intake [$F(3, 51) = 3.33$; $p<0.05$]. Post hoc - OT 1.0mg/kg significantly reduced intake of sucrose (ml/kg) compared to vehicle.	↓ (1mg/kg) ↔ (0.1 and 0.3mg/kg)
King et al. (2017)[12] *USA* Experiment 9	Sucrose intake	Mice C57BL/6J	12	M	9-10 wk	2 x sessions (max 3h)	Reversed 12h light/ 12 h dark cycle	IP OT 3.0mg/kg vs saline, crossover design; injected 30min prior to testing.	Self-administered sucrose by progressive-ratio schedule (increasing requirements to obtain a sucrose reinforcement with each new schedule). Stable response rates on fixed- ratio-4 schedule established prior to testing.	OT did not significantly alter responding for sucrose, and analysis of breakpoint data indicated no significant difference between OT and vehicle conditions, $t(10) = 1.31$, $p > 0.20$.	↔
Klockars et al. (2017a)[73]	Sucrose intake	Rats Sprague-Dawley	11-12/group	M	Adult	2 h	12h light/ 12h dark	IV OT 0.1µg/kg vs. saline; injected prior to testing.	Intake of 10% sucrose solution measured	IV OT 0.1µg/kg did not reduce episodic	↔

NZ & USA Experiment 3							cycle (lights on 0700)		(grams) 1h and 2h post-injection; no access to chow or water.	consumption of sucrose (p>0.05).	
Klockars et al. (2017a)[73] *NZ & USA* Experiment 8	Sucrose intake	Rats Sprague-Dawley	7/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg vs. saline; injected prior to testing.	Intake of palatable sweet chow (58% CHO) measured (grams) 1h and 2h post-injection; no access to standard chow or water.	OT 0.1µg/kg did not reduce episodic intake of solid sweet chow (p>0.05).	↔
Klockars et al. (2017b)[75] *NZ & USA* Experiment 5	Sucrose intake	Rats Sprague-Dawley	11/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VMH OT 1.0µg vs. saline; injected prior to testing.	Intake of 10% sucrose solution measured (grams) 1h and 2h post-injection; no access to chow or water.	2h consumption of sucrose remained unchanged after VMH OT 1.0µg (p>0.05).	↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 3	Sucrose intake	Rats Sprague-Dawley	8-10/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	BLA OT 0.03, 0.1 and 0.3µg vs. saline; injected just before testing.	Intake of 10% sucrose solution measured (grams) 2 h post-injection; no access to chow or water.	BLA OT 0.1 and 0.3µg significantly decreased episodic sucrose intake [F(3, 32)=4.985; p=0.0478 and 0.0462, respectively].	↓ (0.1 and 0.3µg)
Klockars et al. (2018)[74] *NZ & USA* Experiment 4	Sucrose intake	Rats Sprague-Dawley	8/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	CNA OT 1.0µg vs. saline; injected just before testing.	Intake of 10% sucrose solution measured (grams) 2 h post-injection; no access to chow or water.	No significant effect of CNA OT on sucrose intake (p>0.05).	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 12	High sucrose vs. standard diet	Rats Sprague-Dawley	NR	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg OT vs. saline; injected prior to testing.	Following overnight food deprivation, 10% sucrose solution and standard chow presented concurrently, no access to water. Sucrose and chow intake measured (grams) 2h post-injection; chow (grams) and total energy intake (kcal) measured 24h post-injection.	IV OT 0.1 µg/kg did not change sucrose solution intake (p>0.05), but did decrease consumption of chow (p=0.0141), and total energy ingested with combined chow and sucrose solution intake (p=0.0474).	↓ (chow intake) ↔ (sucrose intake)
Klockars et al. (2017b)[75] *NZ & USA*	Sucrose intake	Rats Sprague-Dawley	8/group	M	9 wk	2 h	12h light/ 12h dark cycle	VMH OT 1.0µg vs. saline; injected prior to testing.	Following overnight food deprivation, 10% sucrose solution and standard	VMH OT 1.0µg reduced chow intake (p=0.0105) without affecting	↓ (chow intake)

Experiment 9							(lights on 0800)		chow presented concurrently, no access to water. Sucrose and chow intake measured (grams) 2h post-injection.	sucrose solution intake (p>0.05).	↔ (sucrose intake)
Mullis et al. (2013)[71] *USA* Experiment 1	Sucrose intake	Rats Wistar	10 naïve	M	NR	30 min	12h light/ 12h dark	Intra-VTA OT 0.3, 1 or 3µg vs. saline (crossover design); injection 15 min before testing	Intake of 10% sucrose solution measured (g/30min); no access to food or water	OT significantly reduced sucrose intake by 13.35% - 20.5% [F (3,27) = 6.09, p< 0.01] at 1 and 3µg vs. saline (p<0.05), 0.3µg OT not effective.[a]	↓(1 and 3µg OT) ↔ (0.3µg OT)
Sinclair et al. (2015)[9] *USA* Experiment 1	Sucrose intake	Mice C57BL/9	15	M&F	Adult	3 x 30 min sessions	NR	IP 0.1mg/kg OT vs. saline, crossover design (sessions 1 & 3: saline injection; session 2: OT injection); injected 30 min before testing	Following partial food/water deprivation, 7 bottle choice test: sucrose solution (concentrations 0.03, 0.1, 0.2, 0.3, 0.6 and 1M) and distilled water in a randomized block design. Standard Lick Ratio (SLR) calculated, SLR = lick rate tastant/maximum lick rate.	Licking for sucrose reduced by OT (main effect of Treatment: F(1,14)=20.10, p=0.00052; Treatment × Concentration interaction: F(6,84)=8.60, p<0.0001).[a] Post-hoc tests: significant reduction in sucrose licking at 0.3 M (t(14) = 5.13, p = 0.0011) and NS trend at 0.2 M.	↓
Zhou et al. (2015)[10] *USA* Experiment 1	Sucrose intake	Rats Sprague-Dawley	9-10 (sucrose experienced)	M&F	Adult	2 h	12h dark/ 12h light (lights off 0600)	IP OT 0.1, 0.3, 1.0, and 3.0mg/kg vs. vehicle (crossover design); injected 30 min before testing	Sucrose self-administration (45mg sucrose pellets) using active and inactive lever responding (fixed ratio 1 schedule). Intake measured as number of sucrose pellets earned and mg sucrose/kg BW delivered. Food-restricted (~20g/day) to maintain 85% of ad lib BW.	OT dose dependently decreased lever active lever pressing in both sexes [F(4,68)=8.2, p<0.05]: females = 0.3, 1, and 3mg/kg OT; males =3mg/kg OT (p<0.05). Inactive lever presses reduced with OT [dose main effect, F(4,68)=2.7, p<0.05]; follow up comparisons NS. Males earned more pellets than females [F(1,17)=8.34, p<0.05]. OT decreased pellets earned [F(4,68)=5.7, p<0.05], but no interaction of sex and oxytocin dose. Decreased pellets	↓ Female (0.3, 1, and 3mg/kg OT) ↓ Male (3mg/kg OT)

										earned: females =1mg/kg OT (p<0.05); males = 3mg/kg OT (p<0.05). OT decreased sucrose earned per BW [F(4,68)=7.8, p<0.05], no sex differences or sex × OT dose interaction. Decreased pellets/BW: females =0.3, 1, and 3 mg/kg OT (p<0.05); males =3 mg/kg OT (p<0.05).	
Herisson et al. (2016)[11] *NZ* Experiment 2	Sucrose and saccharin intake	Rats Sprague-Dawley	8-12/group	M	Adult	2 h	12h light/ 12h dark (lights on 0700)	Nucleus accumbens (core or shell) OT 0.1, 0.3, 1 and 3µg vs. saline: injected 5min before feeding.	Intake (g/2 hours) of 10% sucrose solution vs. 0.1% saccharin. Food and water unavailable.	Significant decrease in sucrose solution intake by ~50% at OT (core) doses 1µg (p=0.017) and 3µg (p=0.045). Lower OT (core) doses needed to decrease saccharin solution intake by ~50%: 0.03µg (p=0.03), 0.1µg (p=0.026), 0.3µg (p=0.025) and 1µg (p=0.027).[a]	↓
Klockars et al. (2017a)[73] *NZ & USA* Experiment 5	Sucrose and saccharin intake	Rats Sprague-Dawley	10/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg vs. saline; injected prior to testing.	Intake of "super-sweet" 10% sucrose-0.1% saccharin solution measured (grams) 1 h and 2 h post-injection; no access to chow or water.	IV OT 0.1µg/kg did not reduce episodic consumption of "super-sweet" solution (p>0.05).	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 7	Sucrose and saccharin intake	Rats Sprague-Dawley	7/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.3µg/kg vs. saline; injected prior to testing.	Intake of "super-sweet" 10% sucrose-0.1% saccharin solution measured (grams) 2h post-injection; no access to chow or water.	IV OT 0.3µg/kg did not reduce episodic consumption of "super-sweet" solution (p>0.05).	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 4	Saccharin intake	Rats Sprague-Dawley	6/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg vs. saline; injected prior to testing.	Intake of 0.1% saccharin solution measured (grams) 1 h and 2 h post-injection; no access to chow or water.	IV OT 0.1 µg/kg did not reduce episodic consumption of saccharin (p>0.05).	↔
Klockars et al. (2017b)[75] *NZ & USA*	Saccharin intake	Rats Sprague-Dawley	6/group	M	9 wk	2 h	12h light/ 12h dark cycle	VMH OT 1.0µg vs. saline; injected prior to testing.	Intake of 0.1% saccharin solution measured (grams) 1h and 2h post-	2h consumption of saccharin remained	↔

Experiment 6							(lights on 0800)		injection; no access to chow or water.	unchanged after VMH OT 1.0µg (p>0.05).	
Klockars et al. (2018) *NZ & USA* Experiment 5	Saccharin intake	Rats Sprague-Dawley	8-9/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	BLA OT 0.1, 0.3 and 1.0µg vs. saline; injected just before testing.	Intake of 0.1% saccharin solution measured (grams) 2 h post-injection; no access to chow or water.	BLA OT 1.0µg significantly decreased episodic saccharin intake [F(3, 21)=5.271, p=0.0076].	↓ (1.0µg)
Klockars et al. (2018)[74] *NZ & USA* Experiment 6	Saccharin intake	Rats Sprague-Dawley	8-9/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	CNA OT 1.0µg vs. saline; injected just before testing.	Intake of 0.1% saccharin solution measured (grams) 2 h post-injection; no access to chow or water.	No significant effect of CNA OT on saccharin intake (p>0.05).	↔
MacFadyen et al. (2016)[47] *USA* Experiment 1	Saccharin intake	Rats Sprague-Dawley	NR	M	NR	2 h	12h light/ 12h dark (lights on 2300)	IP OT 0.05, 0.1, 0.3, and 0.5 mg/kg, crossover design. Injection 30 min prior to bottle test. 4 consecutive days of saline injections between tests.	Three-bottle choice: 0.05% saccharine, 10% ethanol in 0.05% saccharine, and 15% ethanol in 0.05% saccharine, 3 h into dark cycle. Saccharin intake measured (ml/kg). Baseline consumption levels established prior to testing.	No significant effect of OT on saccharine consumption compared to saline [F(2,6) = 1.5; p>0.1.[a]	↔
Blevins et al. (2016)[16] *USA* Experiment 3	Saccharin preference	Rat Sprague-Dawley CD® IGS*	7-9/group DIO (treatment and vehicle)	M	~2.5-6 mo	2 h	12h light/ 12h dark (lights on at 1300)	SC OT infusion via 14 d mini pump of varying doses: 50nmol/day vs. 100nmol/day vs. 200nmol/day vs. saline	Day 4 two-bottle 2 h saccharin (0.1%) preference test (preference ratio) onset of dark cycle.	OT (50, 100, 200 nmol/day) did not significantly alter 2-h saccharin preference ratios compared to vehicle.	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 13	Sucrose vs. lipid preference	Rats Sprague-Dawley	8/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg OT vs. saline; injected prior to testing.	Intralipid and 10% sucrose solution presented concurrently, no access to chow or water. Intakes (intake ratio and kcal) measured 2h post-injection.	IV OT 0.1 µg/kg did not change cumulative amount of the two tastants consumed or the Intralipid-to-sucrose intake ratio (p>0.05).	↔
Blevins et al. (2016)[16] *USA* Experiment 4	High fat vs. standard diet	Rat Sprague-Dawley CD® IGS	5-6/group (treatment and vehicle)	M	~2.5-6 mo	26 d	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline vs. control	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat). Food available ad lib, intake recorded daily (kcal/day).	OT had a significant effect on sustained reduction of energy intake in HFD-fed vs. vehicle. OT significantly reduced energy intake	↓

										in HFD-fed vs. to chow-fed controls ($p<0.05$).[a]	
Blevins et al. (2016)[16] *USA* Experiment 5	High fat vs. standard diet	Rat Sprague-Dawley CD® IGS	6-8/group (treatment and vehicle)	M	~2.5-6 mo	26 d	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline vs. control	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat) in progressing DIO (ad lib fed rats maintained on chow or HFD for 2 and 2.5 mo before testing). Food available ad lib, intake recorded daily (kcal/day).	Non-significant reduction in energy intake in HFD-fed vs. vehicle; no significant effect on energy intake in chow-fed vs. vehicle ($p>0.05$).[a] Non-significant diet-drug interactive effect for OT to reduce energy intake in HFD-fed vs. chow-fed on day 22 ($p=0.060$).	↔
Blevins et al. (2016)[16] *USA* Experiment 6	High fat vs. standard diet	Rat Sprague-Dawley-CD® IGS	7-8/group DIO (treatment and vehicle)	M	~2.5-6 mo	21 d	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat) in DIO (ad lib fed rats maintained on chow or HFD for 4 and 4.5 mo before testing). Food available ad lib, daily intake (kcal/day) recorded days 1–5 and 21, 72 h measurements completed between days 9 and 12.	HFD-fed vs. vehicle transient reduction in energy intake during days 1–5, days 9-12, no longer significant by day 21 ($p>0.05$).[a] OT had no significant effect on energy intake in chow-fed vs. vehicle. Significant diet-drug interactive effect for OT to reduce energy intake in HFD-fed vs. chow-fed controls on days 4-5 ($p<0.005$).	↔
Blevins et al. (2016)[16] *USA* Experiment 7	High fat diet lacking sucrose	Rat Sprague-Dawley CD® IGS	8-10/group DIO (treatment and vehicle)	M	~2.5-6 mo	28 d	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline	HFD (60% kcal from fat) lacking sucrose in DIO (ad lib fed rats maintained on HFD lacking sucrose for 4 and 4.5 mo before testing). Daily food intake recorded (kcal/day) in 3 h fasted rats.	OT reduced energy intake, maintained until third week of study ($p<0.05$).[a]	↓
Blevins et al. (2016)[16] *USA* Experiment 8	High fat vs. standard diet	Rat Sprague-Dawley SD-SAS	6-12/group (treatment and vehicle)	M	~2.5-6 mo	13 d	12h light/ 12h dark (lights on at 1300)	SC OT infusion via 14 d mini pump: 50nmol/day vs. saline; serum OT measured day 13	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat). Food available ad lib, intake recorded daily (kcal/day).	Reduced energy intake in HFD-fed vs. chow-fed controls across days 2 and 4 ($p<0.05$).[a]	↔

Maejima et al. (2011)[55] *Japan* Experiment 3	High fat diet	Mice C57BL/6J	5/group	M	6 wk	24 h	12h light/ 12h dark cycle (lights on 0700)	SC OT 1,600µg/kg vs. vehicle (saline); injected 2 h before start of dark phase/feeding.	Cumulative food intake (grams) 1, 2, 3, 6 and 24 h measured. Food (HFD chow) and water available ad lib.	SC OT 1,600µg/kg significantly suppressed HFD intake for 1 to 24 h, compared to vehicle($p<0.01$).	↓
Maejima et al. (2011)[55] *Japan* Experiment 4	High fat diet	Mice C57BL/6J	5/group	F	6 wk	17 d	12h light/ 12h dark cycle (lights on 0700)	Daily SC OT 1,600 µg/kg for 17 days; injected 2 h before start of dark phase/feeding.	Daily and cumulative food intake (grams) measured. Food (HFD chow) and water available ad lib.	Daily SC OT 1,600 µg/kg decreased daily food intake for up to day 6 ($p<0.01$). Days 7-17 no significant difference between control and OT groups.	↓ (Days 1-6)
Maejima et al. (2011)[55] *Japan* Experiment 5	High fat diet	Mice C57BL/6J	11 DIO control 14 DIO treatment	M&F	6 wk	14 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 1,600 µg/kg/day vs. saline	Daily and cumulative food intake (grams) measured. Food (HFD chow) and water available ad lib.	Chronic OT 1,600 µg/kg/day infusion decreased food intake for first 6 days (statistically significant difference obtained at days 3 and 4, $p<0.05$).	↓ (Days 1-6)
Maejima et al. (2017)[58] *Japan* Experiment 1	High fat diet	Mice C57BL/6J	19 DIO control 19 DIO treatment	M	14 wk (M) 18 wk (F)	10 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 800 or 1,600 µg/kg/day vs. saline [specific OT dose not reported].	Mice maintained on HFD; 24 h food intake measured (grams) everyday at 17:00 (2 h before onset of dark phase).	OT significantly decreased food intake compared to control, $F(1,324)= 47.66$, $p<0.01$.	↓
Maejima et al. (2017)[58] *Japan* Experiment 2	High fat diet	Mice C57BL/6J	19 DIO control 20 DIO treatment	F	14 wk (M) 18 wk (F)	10 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 800 or 1,600 µg/kg/day vs. saline [specific OT dose not reported].	Mice maintained on HFD; 24 h food intake measured (grams) everyday at 17:00 (2 h before onset of dark phase).	OT significantly decreased food intake compared to control, $F(1,333)=23.37$, $p< 0.01$.	↓
Maejima et al. (2017)[58] *Japan* Experiment 5	High fat diet	Mice C57BL/6J	DIO Male: 6 control 5 OT 800µg/kg 5 OT 1600µg/kg DIO Female: 6 control 7 OT 800µg/kg 7 OT 1600µg/kg	M&F	14 wk (M) 18 wk (F)	10 d	12h light/ 12h dark cycle (lights on 0700)	SC infusion via 14d mini pump: OT 800 and 1,600 µg/kg/day vs. saline.	Mice maintained on HFD. 24 h food intake measured (grams) everyday at 17:00 (2h before onset of dark phase).	In males OT infusion had no significant effect on food intake ($p>0.05$). In females OT infusion decreased food intake dose dependently with significant differences obtained at days 4 (OT 800µg/kg, $p<0.05$; OT 1600µg/kg, $p<0.01$) and	↔ (male & female) ↓ (female: days 4 & 5)

										5 (OT 1600µg/kg, p<0.01) only.	
Roberts et al. (2017)[57] *USA* Experiment 1	High fat vs. standard diet	Rats Long Evans	HFD 17-18/group (treatment and vehicle) Standard diet 6-7/group (treatment and vehicle)	M	~5.25-6.5 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. vehicle (saline)	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat) in DIO (ad lib fed rats maintained on chow or HFD for 4 and 4.5 mo before testing). Food available ad lib, daily intake (kcal/day) recorded.	OT had a significant effect on sustained reduction of energy intake in HFD-fed treatment vs. vehicle ($p<0.05$). In chow-fed controls OT had no effect on energy intake in treatment vs. vehicle groups ($p>0.05$).	↓ HFD ↔ standard diet
Roberts et al. (2017)[57] *USA* Experiment 2	High fat vs. standard diet	Rats Long Evans	7-11/group	M	~6.6-7.5 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	Effects of treatment cessation i.e. no OT infusion (mini pump removed from experimental DIO rats after 27 days OT treatment)	Daily food intake recorded (kcal/day) in 3h fasted rats.	Apart from 'rebound hyperphagia' developed during the 2nd wk following minipump removal, no significant difference in food intake between post-oxytocin vs. post-vehicle groups.	↔
Roberts et al. (2017)[57] *USA* Experiment 3	High fat vs. standard diet	Mice C57BL/6J	HFD 7-12/group (treatment and vehicle) Standard diet 8-9/group (treatment and vehicle)	M	~6.6-7.5 mo	28 d	12h dark/ 12h light cycle (lights off 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. vehicle (saline)	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat) in DIO (ad lib fed mice maintained on chow or HFD for 4 and 4.5 mo before testing). Food available ad lib, daily intake (kcal/day) recorded.	HFD-fed vs. vehicle reduction in energy intake during first 2 wk ($p<0.05$). No significant changes in energy intake in chow-fed vs. vehicle ($p>0.05$).	↓ 2 wk (HFD)
Roberts et al. (2017)[57] *USA* Experiment 5	High fat vs. standard diet	Rats Sprague-Dawley CD® IGS	HFD 12-15/group (treatment and vehicle) Standard diet 7-11/group (treatment and vehicle)	M	~3-9.25 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	4V infusion via 27d mini pump: OT 16nmol/day vs. vehicle (saline)	Intake of HFD (60% kcal from fat) vs. chow (13% kcal from fat) in DIO (ad lib fed mice maintained on chow or HFD for 4 and 4.5 mo before testing). Food available ad lib, daily intake (kcal/day) recorded.	HFD-fed vs. vehicle sustained reduction in energy intake during first 3 wk ($p<0.05$). Significant effect on energy intake in chow-fed vs. vehicle over 4-day period during first wk only ($p<0.05$).	↓
Roberts et al. (2017)[57] *USA*	High fat vs. standard diet	Rats Sprague-Dawley CD® IGS	6/group	M	~5.25-6.5 mo	27 d	12h dark/ 12h light cycle	Effects of treatment cessation i.e. no OT infusion (mini pump removed from	Daily food intake recorded (kcal/day) in 3 h fasted rats.	No significant difference in food intake between post-	↔

Experiment 7							(lights off 1300)	experimental DIO rats after 27 days OT treatment)		oxytocin vs. post-vehicle groups.	
Roberts et al. (2017)[57] *USA* Experiment 8	High fat diet	Rats Long Evans	6-8/group	M	~6.6-7.5 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	4V infusion via 28d mini pump: OT 16nmol/day vs. vehicle (saline)	Intake of HFD (60% kcal from fat) in DIO (ad lib fed mice maintained on HFD for 4 and 4.5 mo before testing). Food available ad lib, daily intake (kcal/day) recorded.	HFD-fed vs. vehicle sustained reduction in energy intake.	↓
Roberts et al. (2017)[57] *USA* Experiment 9	High fat diet	Rats Long Evans		M	~6.6-7.5 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	Effects of treatment cessation i.e. no OT infusion (mini pump removed from experimental DIO rats after 27 days OT treatment)	Daily food intake recorded (kcal/day) in 3 h fasted rats.	Apart from transient increase in energy intake evident in 3rd wk, no significant difference in food intake between post-oxytocin vs. post-vehicle groups.	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 6	Palatable high fat emulsion intake	Rats Sprague-Dawley	7-8/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.1µg/kg vs. saline; injected prior to testing.	Intake of 4.1% Intralipid emulsion measured (grams) 1h and 2h post-injection; no access to chow or water.	IV OT 0.1µg/kg did not reduce episodic consumption of Intralipid (p>0.05).	↔
Bernal et al. (2007)[65] *Spain* Experiment 2	Low sodium diet	Rats Wistar	24 (8/group)	M	Adult	4 d	12h light/ 12h dark (lights on 0800)	SC 0.5mL OT 5IU/mL vs. OT 10IUmL vs. vehicle (distilled water); injected on day 3 at 0830 and 1430 h.	Day 1: 24 h baseline period, with ad lib access to standard chow and water. Days 2-4: chow replaced with low sodium diet (0.04% Na) for 72 h. Food intake recorded (g/day).	Baseline (chow g/day) – Day 1: Control = 23.3±1.9, OT 5IU = 23.8±2.0, OT 10IU = 22.6±1.42. Low sodium diet (g/day) – Day 2: Control = 13.2±2.0, OT 5IU = 13.2±2.0, OT 10IU = 13.6±1.8; Day 3: Control = 18.8±1.0, OT 5IU = 17.2±1.6, OT 10IU = 19.8±1.2; Day 4: Control = 17.8±0.5, OT 5IU = 15.2±1, , OT 10IU = 15.2±1.1. No differences in food intake 1st 72 h between groups. Non-significant reduction in 24 h food intake following OT	↔

										administration [F statistics not reported].	
King et al. (2017)[12] USA Experiment 1	Alcohol intake	Mice C57BL/6J	40 (10/group)	M	9-10 wk	4 h	Reversed 12h light/ 12h dark cycle	Day 4: IP OT 1, 3, 10mg/kg vs saline; injected 30min before access to EtOH.	Days 1-3: daily 2 h access to single 15mL bottle of 20% (v/v) EtOH 3h into dark phase. Day 4: access to EtOH for 4 h.	Significant effect of dose on EtOH consumption [F(3,36) = 12.31; p<0.0001]; significant decrease in consumption for 3mg/kg (p<0.05) and 10mg/kg (p<0.01) OT compared to vehicle.	↓ (3 and 10mg/kg OT)
King et al. (2017)[12] USA Experiment 2	Alcohol intake	Mice C57BL/6J	40 (10/group)	M	9-10 wk	4 h	Reversed 12h light/ 12h dark cycle	Day 4: IP OT 0.3, 1.0, 3.0mg/kg vs saline; injected 30min before access to EtOH.	Days 1-3: daily 2 h access to single 15mL bottle of 20% (v/v) EtOH 3 h into dark phase. Day 4: access to EtOH for 4 h.	Significant effect of dose on EtOH consumption [F(3,19) = 35.18; p<0.0001]; significant decrease in consumption for 0.3, 1.0 and 3.0mg/kg (all p<0.01) OT compared to vehicle, with higher doses more effective.	↓
King et al. (2017)[12] USA Experiment 3	Alcohol intake	Mice C57BL/6J	24 (5-6/group)	M	9-10 wk	24 h	Reversed 12h light/ 12h dark cycle	Day 4: IP OT 1, 3, 10mg/kg vs saline; injected 30min before access to EtOH.	Days 1-3: daily 2 h access to 20% (v/v) EtOH bottle fitted with lickometer 3h into dark phase. Day 4: access to EtOH for 4 h.	OT decreased licking responses at 3 (p<0.05) and 10mg/kg (p<0.01) doses. OT treatment delayed first contact with EtOH bottle by 1-2 h. Significant main effects of OT Dose [F(3,18) = 30.88; p<0.0001], and Time [F(23, 414) = 57.10; p<0.0001], and Dose x Time interaction [F(69, 414) = 5.03; p<0.0001]. Post hoc analyses - all 3 OT doses significantly decreased EtOH lick contacts compared to saline over entire 4 h drinking session.	↓
King et al. (2017)[12] USA Experiment 5	Alcohol intake	Mice C57BL/6J	12	M	9-10 wk	24 h	Reversed 12h light/ 12h dark cycle	IP OT 1.0mg/kg vs saline; injected prior to EtOH access.	Two-bottle choice: 20% EtOH or water, 24 h unlimited access. Stable daily consumption levels established prior to	OT significantly reduced EtOH intake 4 h post-injection, ml: F(1, 11) = 5.92; p<0.05, and g/kg: F(1, 11) = 6.16; p<0.05	↓

									testing (3wk period). Intake measured at 4 and 24 h.	over 24 h, ml: F(1, 11) = 20.39; p<0.001, and g/kg: F(1, 11) = 20.87; p<0.001.	
King et al. (2017)[12] USA Experiment 6	Alcohol intake	Mice C57BL/6J	13	M	9-10 wk	20min sessions	Reversed 12h light/ 12h dark cycle	IP OT 0.1, 0.3 and 1.0mg/kg vs. saline, crossover design; injections 30min prior to operant sessions.	Operant self-administered by 2 lever press (active/inactive): 12% unsweetened EtOH intake (g/kg) measured. Stable response rates on fixed- ratio-4 schedule established prior to testing.	OT significantly reduced EtOH responding (0.1 and 0.3mg/kg, p<0.05; 1.0mg/kg, p<0.001) and intake (0.1and 0.3 mg/kg, p<0.01; 1 mg/kg, p<0.001) compared to vehicle condition.	↓
King et al. (2017)[12] USA Experiment 7	Alcohol intake	Mice C57BL/6J	10	M	9-10 wk	2 x sessions (max 3 h)	Reversed 12h light/ 12h dark cycle	IP OT 3.0mg/kg vs saline, crossover design; injected 30min prior to testing.	Self-administered EtOH by progressive-ratio (PR) schedule (increasing requirements to obtain a EtOH reinforcement with each new schedule). Stable response rates on fixed- ratio-4 schedule established prior to testing.	OT decreased overall active lever responding during PR sessions. OT significantly reduced breakpoint ratio achieved for EtOH reward compared to vehicle, t(8) = 2.82, p < 0.03.	↓
MacFadyen et al. (2016)[47] *USA* Experiment 2	Alcohol intake	Rats Sprague-Dawley	NR	M	NR	2 h	12h light/ 12h dark (lights on 2300)	IP OT 0.05, 0.1, 0.3, and 0.5 mg/kg, crossover design. Injection 30 min prior to bottle test. 4 consecutive days of saline injections between tests.	Three-bottle choice: 0.05% saccharine, 10% ethanol in 0.05% saccharine, and 15% ethanol in 0.05% saccharine, 3 h into dark cycle. Alcohol intake measured (g/kg/2 h). Baseline consumption levels established prior to testing.	OT (all doses) decreased total ethanol intake by ~40%. Significant effect of treatment on ethanol consumption [F(2,6) = 29.88; p<0.005].[a] No significant effect of OT on saccharine consumption compared to saline [F(2,6) = 1.5; p>0.1.[a]	↓
MacFadyen et al. (2016)[47] *USA* Experiment 3	Alcohol intake	Rats Sprague-Dawley	6 plain gel 6 ethanol gel	M	NR	7 x 30min	12h light/ 12h dark (lights on 0600)	IP OT 0.3 mg/kg vs. saline, crossover design; injections 30min prior to operant session.	Operant self-administered: 10% ethanol gelatin vs. plain gelatin Gelatin intake (g/kg/30 min) and calorie consumption (cal/kg/30 min) measured.	OT decreased ethanol gel consumption by ~30% and decreased plain gel consumption by <10%. Significant treatment by gel type interaction [F(1,10)=7.94, p<0.05].[a] OT decreased ethanol intake from ~1.2 g/kg to 0.75 g/kg.[a] Significantly higher calories	↓

										consumed per kg BW when rats had ethanol gel compared to plain gel. OT reduced caloric consumption in ethanol gel group to that of plain gel group.	
Peters et al. (2012)[40] *Germany Experiment 1*	Alcohol intake	Mice C57BL/6N	6-7 stressed (undergone 14-day chronic subordinate colony housing stress paradigm) 6-7 controls (single house controls)	M	NR	24 h	12h light/ 12h dark (lights on 0600)	IP OT 10mg/kg OT vs. vehicle (Ringer solution, pH 7.4), within-subject design; injected 15 min before testing (start of dark phase).	Two-bottle choice test: 8% EtOH vs. water, intake recorded. Consumed alcohol (g/kg) compared with 3-day mean baseline (%).Test repeated after 72 h washout with bottle order reversed.	Prior to intervention stressed mice consumed significantly more EtOH than controls ($p<0.05$).[a] OT vs. vehicle significantly reduced EtOH intake in controls ($p<0.05$).[a] OT had no effect on stressed mice i.e. OT did not reduce stress-induced EtOH consumption.	↓ (controls) ↔ (stressed mice)
Peters et al. (2012)[40] *Germany* Experiment 2	Alcohol intake	Mice C57BL/6N	24 CSC (undergone 14-day stress paradigm: chronic subordinate colony housing) 23 SHC (single house controls)	M	NR	24 h	12h light/ 12h dark (lights on 0600)	ICV LV 0.5µg/2µL OT vs. vehicle (Ringer solution, pH 7.4), within-subject design; injected 15 min before testing (start of dark phase).	Two-bottle choice test: 8% EtOH vs. water, intake recorded. Consumed alcohol (g/kg) compared with 3-day mean baseline (%). Test repeated after 72 h washout with bottle order reversed.	Prior to intervention stressed mice consumed significantly more EtOH than controls ($p<0.05$).[a] OT vs. vehicle had not effect on EtOH consumption in either group ($p>0.05$).[a]	↔
Peters et al. (2017)[72] *Germany*	Alcohol intake	Rats Wistar	15 treatment 11 vehicle	M	NR	60 d (29 drinking sessions)	12h light/ 12h dark (lights on 0600)	ICV LV OT 1µg/5µL vs. vehicle (Ringer solution, pH 7.4); injected 10 min before testing (day 28).	EtOH intake recorded during 27 pre-treatment drinking sessions and 29th session following treatment session. Treatment session = 28th drinking session: two-bottle choice test: EtOH (20% v/v in water) vs. water, 24 h intake recorded (g/kg).	EtOH consumption: no difference between groups in pre-treatment drinking session (session 27; $p=0.775$) or following (session 29; $p=0.623$) treatment session (session 28).[a] OT-treated rats consumed less during treatment session compared with prior drinking session [$F_{1,14}=38.77$, $p<0.001$] and compared with vehicle-treated rats [$F_{1,24}=6.13$, $p=0.021$]; interaction:	↓

										[F1,24=8.03, p=0.009].[a] No change in consumption after vehicle treatment (p=0.095).[a]	
Sinclair et al. (2015)[9] *USA* Experiment 2	Taste responses to aversive (bitter, sour, salty) and appetitive (sweet, umani) stimuli	Mice C57BL/8	12	M&F	Adult	6 x 20min sessions	NR	IP 10mg/kg OT vs. saline, crossover design; injected 30 min before testing	Following 24 h water deprivation, 6 bottle choice test: 1) 300mM NaCl; 2) 20mM citric acid; 3) 0.3mM quinine-HCl; 4) 10mM Na-saccharin; 5) 100mM monosodium glutamate (MSG) + 0.5mM inosine monophosphate (IMP); and 6) distilled water; tastants randomly presented. Lick rates for tastants relative to water, and raw lick rates (5s) measured.	No differences in lick ratios between OT and saline conditions for NaCl (t(11) = −0.686, p=0.507), citric acid (t(11) = −0.475, p=0.644), and quinine (t(11) = 1.266, p=0.232) unaffected by OT.[a] OT increased preference for saccharin (t(11) = −3.691, p=0.0036) and MSG + IMP (t(11) = −2.468, p=0.031) relative to water.[a] Raw lick rates for water and all taste stimuli depressed following OT injection (significant effect of Drug [(1,7)=47.993, p=0.00023].[a]	↓
Blevins et al. (2016)[16] *USA* Experiment 9	Kaolin intake (aversive drug effects)	Rat Sprague-Dawley CD® IGS	6-8/group (treatment and vehicle)	M	~2.5-6 mo	15 d	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline	Kaolin intake, placement of kaolin (non-nutritive substance) and chow reversed every other day within each treatment condition. Food available ad lib, intake recorded daily.	OT failed to increase kaolin consumption (data not shown), suppression of food intake was not secondary to an aversive effect of central OT.	↓
Blevins et al. (2016)[16] *USA* Experiment 10	Kaolin intake (aversive drug effects)	Rat Sprague-Dawley SD-SAS	6-10/group DIO (treatment and vehicle)	M	~2.5-6 mo	12 d	12h light/ 12h dark (lights on at 1300)	SC OT infusion via 12 d mini pump: 50nmol/day vs. saline	Kaolin intake, placement of kaolin and chow reversed every other day within each treatment condition. Food available ad lib, intake recorded daily (g).	OT (50 nmol/day) produced no significant increase in kaolin consumption.[a] Chronic SC OT administration, at doses that reduce food intake, unlikely to elicit nausea.	↔

Herisson et al. (2016)[11] *NZ* Experiment 3	Conditioned Taste Aversion (CTA)	Rats Sprague-Dawley	5/group	M	Adult	5 d	12h light/ 12h dark (lights on 0700)	Nucleus accumbens (core) OT 1µg or saline given on day 4 after 60min access to saccharine solution.	Day 1-3: water access for 2 h/day (food unavailable), Day 4: novel 0.1% saccharin solution given instead of water for 60 min, Day 5: Two-bottle preference test, saccharin vs. water, to assess if CTA to saccharin present. Relative intake of saccharin recorded.	Similar intakes between treatment and vehicle groups. 1µg dose of OT after presentation of the novel 0.1% saccharin solution did not produce learned avoidance of saccharin in subsequent two-bottle choice test (NS).[a]	↑
Iwasaki et al. (2014)[50] *Japan* Experiment 5	Conditioned Taste Aversion (CTA)	Mice C57BL/6J	12 (4/group)	M	8-12 wk	8 d	12h light/ 12h dark (lights on 0730)	IP OT 200µg/kg vs. saline; injection day 6 after given saccharin.	Day 6 (following 5 day water deprivation schedule): 0.15% saccharin given instead of water for 0.5 h; Day 7: rest day, 2 h of normal water access; Day 8: Two-bottle choice (0.15% saccharine vs. water) for 0.5 h. CTA determined as saccharine preference ratio, saccharin intake/total intake.	OT did not induce conditioned taste aversion (i.e. OT had no influence on saccharin preference).[a]	↔
Noble et al. (2014)[46] *USA* Experiment 4	Conditioned Taste Aversion (CTA)	Rats Sprague-Dawley	6-7/group naïve	M	Adult	24 h	12h light/ 12h dark (lights on 0400)	VHM OT 0.1nmol vs. OT 1.0nmol vs. vehicle (aCSF); injected just before testing. CTA used to test if OT in VHM has aversive properties.	Two-bottle choice test: water vs. 0.1% saccharin, intake recorded (% saccharin of total fluid). Test repeated after 72 h washout with bottle order reversed.	OT did not cause CTA. OT vs. vehicle did not significantly reduce saccharin intake ($p>0.05$). All groups consumed similar amounts of saccharin (75-88% of total fluid intake).	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 14	Conditioned Taste Aversion (CTA)	Rats Sprague-Dawley	9/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV OT 0.3µg/kg vs. saline; injected prior to testing.	Following 18h water deprivation, two-bottle choice: cherry flavoured KoolAid or water. Intake (ratio) measured 2h post-injection.	IV OT 0.3 µg/kg did not induce development of CTA to novel KoolAid solution ($p>0.05$).	↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 11	Conditioned Taste Aversion (CTA)	Rats Sprague-Dawley	5/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	3 conditions: 1) BLA OT 1.0µg vs. saline; 2) CNA OT 1.0µg vs. saline; 3) IP 6mEq LiCl vs. IP saline (positive control). Injected prior to testing.	Day 1-3: 2 h access to water. Day 4: 2 h access to novel cherry flavoured KoolAid instead of water. Day 5: two-bottle choice - KoolAid or water. Intake	BLA or CNA OT did not induce CTA ($p>0.05$). [IP LiCl used as positive control for CTA ($P<0.0001$)]	↔

									(ratio) measured 2 h post-injection.		
Roberts et al. (2017)[57] *USA* Experiment 4	Kaolin intake (aversive drug effects)	Mice C57BL/6J	3-5/group	M	~6.6-7.5 mo	15 d	12h dark/ 12h light cycle (lights off 1300)	3V infusion via 15d mini pump: OT 16nmol/day vs. vehicle (saline)	Kaolin intake, placement of kaolin and chow reversed every other day within each treatment condition. Food available ad lib, intake recorded daily (g).	OT infusion produced no significant increase in kaolin consumption i.e. no aversive drug effect.	↔
Roberts et al. (2017)[57] *USA* Experiment 6	Kaolin intake (aversive drug effects)	Rats Sprague-Dawley CD® IGS	NR	M	~3-9.25 mo	27 d	12h dark/ 12h light cycle (lights off 1300)	4V infusion via 27d mini pump: OT 16nmol/day vs. vehicle (saline)	Kaolin intake, placement of kaolin and chow reversed every other day within each treatment condition. Food available ad lib, intake recorded daily (g).	OT failed to increase kaolin consumption (data not shown), suppression of food intake was not secondary to an aversive effect of central OT.	↔
Arletti et al. (1989)[13] *Italy* Experiment 2	Food intake and feeding behaviour	Rat Sprague-Dawley	33 (11/group)	M	NR	1 h	Natural light-dark cycle	3 test conditions: 1) ICV OT 1µg/rat vs. 2) ICV OT 10 µg/rat vs. 3) ICV saline; injected 5min before feeding.	Food intake (standard chow) measured (g/hour), latency to 1st meal (sec), meal duration (sec) and no. of meals, following 21h fast.	Food intake (g): saline= 5.68±0.57, 1µg OT= 4.23±1.26, 10µg OT= 2.08±0.32, $F(2,31)=12.78$, $p<0.0001$; latency to 1st meal (sec) : saline= 300.07±67.24, 1µg= 912.12±189.30, 10µg= 2021.43±222.64, $F(2,3)=25.53$, $p<0.00001$; duration (sec): saline= 1932.67±196.52, 1µg= 1733.20±277.54, 10µg= 754.70±114.20, $F(2,31)=13.70$, $p<0.001$, no. of meals: saline= 10.80±1.30, 1µg= 7.40±1.99, 10µg= 7.14±1.41. Dose of 1µg/rat vs. saline, increased latency to first meal ($p<0.05$); dose of 10µg/rat vs. saline or 1µg OT dose, significantly reduced	↓ intake ↓ duration ↑ latency

										duration of feeding, amount of food consumed and increased latency to first meal (all p<0.05).	
Arletti et al. (1989)[13] *Italy* Experiment 4	Food intake and feeding behaviour	Rat Sprague-Dawley	65 [Saline n=12, OT 375 n=6, OT 750 n=8, OT 1500 n=19, OT 3000 n=12, OT 6000 n=8]	M	NR	1 h	Natural light-dark cycle	6 test conditions: 1) IP OT 375µg/kg vs. 2) IP OT 750µg/kg vs. 3) IP OT 1500µg/kg vs. 4) IP OT 3000µg/kg vs. 3) IP OT 6000µg/kg vs. 6) IP saline; injected 30min before feeding.	Food intake (standard chow) measured (g/hour), latency to 1st meal (sec), meal duration (sec) and no. of meals, following 21h fast.	Food intake (g): saline= 11.61±0.42, OT 375µg = 7.43±0.82, OT 750µg = 4.54±0.93, OT 1500µg = 3.44±0.52, OT 3000µg = 3.34±0.71, OT 6000µg = 2.64±0.72, F(5,59)=24.51, p<0.00001; latency to 1st meal (sec) : saline= 76.08±16.51, OT 375µg = 358.80±176.35, OT 750µg = 1054.00±202.70, OT 1500µg = 1063..26±240.42, OT 3000µg = 1115.42±135.30, OT 6000µg = 1502.50±443.18, F(5,59)=4.79, p<0.001; duration (sec): saline= 2973.50±95.54, OT 375µg = 2251.67±49.01, OT 750µg = 1592.25±230.77, OT 1500µg = 1526.26±222.82, OT 3000µg = 1357.00±181.73, OT 6000µg = 1239.25±279.63, F(5,59)=9.12, p<0.00001; no. of meals: saline= 5.75±0.43, OT 375µg = 8.00±0.82, OT 750µg = 6.88±0.87, OT 1500µg = 7.21±0.85, OT 3000µg = 7.83±1.31, OT 6000µg = 7.75±1.25.[b] Dose-	↓ intake ↓ duration ↑ latency

										dependently inhibiting feeding behavior: time spent eating was significantly reduced and latency to the first meal significantly increased, starting from the dose of 750 µ/kg (all p<0.05), while the total amount of food eaten was significantly reduced starting from the dose of 375µg/kg (all p<0.05).	
Arletti et al. (1990)[14] *Italy* Experiment 5	Food intake and feeding behaviour	Rat Sprague-Dawley	33 [Saline n=12, OT 375 n=6, OT 750 n=8, OT 1500 n=19]	M	NR	1 h	Natural light-dark cycle	4 test conditions: 1) IP OT 375µg/kg vs. 2) IP OT 750µg/kg vs. 3) IP OT 1500µg/kg vs. 4) IP saline.	Food intake (standard chow) measured (g/hour), latency to 1st meal (sec), meal duration (sec) and no. of meals, following 21h fast.	Food intake (mg/g BW): saline= 33.17±3.70, OT 375µg = 21.23±2.12, OT 750µg = 12.97±1.98, OT 1500µg = 9.83±1.37, F(3,41)=11.15, p<0.00001; latency to 1st meal (sec) : saline= 76.08±16.51, OT 375µg = 358.80±76.35, OT 750µg = 1054.00±202.70, OT 1500µg = 1063..26±240.42, F(3,41)=5.45, p<0.001; duration (sec): saline= 2973.50±95.54, OT 375µg = 2251.67±49.01, OT 750µg = 1592.25±230.77, OT 1500µg = 1526.26±222.82, F(3,41)=39.18, p<0.00001; no. of meals: saline= 5.75±0.43, OT 375µg = 8.00±0.82, OT 750µg = 6.88±0.87, OT 1500µg = 7.21±0.85. IP OT non-significant reduction in food intake at dose of 375µg/kg (p>0.05). Significant reduction at	↓ intake ↓ duration ↑ latency

										750 and 1500µg/kg ($p<0.05$) in food intake, time spent eating and increased the latency to 1st meal; number of meals not modified.	
Benelli et al. (1991)[15] *Italy* Experiment 3	Food intake and feeding behaviour	Rats Wistar	12 M & 10 F per group	M & F	Adult	1 h	Natural light-dark cycle	4 test conditions: 1) IP OT 375µl/kg vs. 2) IP OT 750µl/kg vs. 3) IP OT 1500µl/kg vs. 4) IP saline; injected 30min before feeding	Male and female food intake (standard chow) measured (mg/g BW), latency to 1st meal (sec), meal duration (sec) and no. of meals, following 21h fast.	Food intake (g)[b] – saline: M= 33.2±3.7, F=31.0±4.1; OT 375µl: M= 21.2±2.1, F=17.1±2.0; OT750µl: M=12.9±1.9, F= 12.2±2.7; OT 1500µl: M=9.8±1.4, F=11.6±1.2. Latency[b] – saline: M= 76.1±16.5, F=65.3±18.3; OT 375µl: M= 358.8±76.3, F=333.1±99.8; OT750µl: M=1054.0±202.7, F= 1011.8±215.6; OT 1500µl: M=1063.3±240.4, F=923.9±179.7. Duration[b] – saline: M= 2973.5±95.5, F=3040.3±103.2; OT 375µl: M= 2251.7±49.0, F=2083.3±65.4; OT750µl: M=1592.2±230.7, F= 1366.3±156.0; OT 1500µl: M=1526.3±222.8, F=1400.7±251.6. No. of meals[b] – saline: M= 5.7±0.4, F=7.8±0.8; OT 375µl: M= 8.0±0.8, F=9.2±0.8; OT750µl: M=6.9±0.9, F= 6.3±0.7; OT 1500µl: M=7.2±0.8, F=5.7±0.6. Doses of 750 and 1500µg/kg vs. saline, decreased food intake and duration of meal, and increased latency to	↓ intake ↓ duration ↑ latency

										first meal in males and females (all p<0.05). No significant effect on no. of meals.	
Blevins et al. (2016)[16] *USA* Experiment 11	Food intake and feeding behaviour	Rat Sprague-Dawley CD® IGS	7-8/group DIO (treatment and vehicle)	M	Adult	72 h	12h light/ 12h dark (lights on at 1300)	3V infusion via 28 d mini pump: OT 16nmol/day vs. saline	HFD in DIO (ad lib fed rats maintained on a HFD for 4 and 4.5 mo before testing). Food available ad lib. Continuous measurement (via calorimetry cages) of energy intake (kcal/day) for meal pattern analysis (size, duration and frequency) between infusion days 12 and 14.	OT reduced meal size during light cycle [F(1,12)=8.831, p<0.05], dark cycle [F(1,12)=5.173, p<0.05], and throughout entire day [F(1,12)=9.778, p<0.05].[a] OT produced shorter meal duration and longer inter-meal interval,[a] with no change in meal frequency i.e. total number of meals consumed not different between treatment and vehicle groups.	↓food intake, size and duration, ↔ frequency
Herisson et al. (2016)[11] *NZ* Experiment 4	Food intake in social setting	Rats Sprague-Dawley	8-10/group	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	Nucleus accumbens (core) OT 1 or 3 µg vs. saline, rats paired (1 treatment + 1 vehicle); injected 5min before feeding.	Food intake (standard chow) measured (grams), following overnight food deprivation.	OT had no effect on hunger-driven food intake in social context of a 1-h meal.[a]	↔
Herisson et al. (2016)[11] *NZ* Experiment 5	Sucrose and saccharin intake in social setting	Rats Sprague-Dawley	6-8/group (treatment and vehicle)	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	Sucrose tests - nucleus accumbens (core) OT 0.03, 0.1, 0.3 or 1µg vs. saline; Saccharin tests: nucleus accumbens (core) OT 0.03, 0.1 or 0.3µg vs. saline. Rats paired (1 treatment + 1 vehicle); injected 5min before feeding.	Intake of 10% sucrose solution vs. 0.1% saccharin measured (grams). Food and water unavailable.	OT had no effect on reward-driven intake in social context of a 1-h meal.[a]	↔
Cox et al. (2013)[52] *USA*	Sucrose reinforced operant conditioning	Rats Long-Evans	7 male 12 female	M & F	NR	NA	12h dark/ 12h light	IP OT 1mg/kg or vehicle (saline) pre-treatment before 6 reinstatement tests	Active lever responding during sucrose self-administration followed by 6 reinstatement tests: cue-induced and sucrose-primed (sucrose pellet every 2 min for 10 min, then one pellet every 30min thereafter) triggers. Standard chow and water available ad lib.	Cue-induced test: females responded more on the active lever than males [F(1,13)=6.97 p<0.05], OT decreased cue-induced reinstatement in females (NS), but not males. Sucrose prime test (natural reward): OT decreased active lever responding in both	↔ (cue-induced reward) ↓ (decreased seeking for natural reward)

										females and males [F(1,13)=8.61, p<0.05]. Females responded more during the sucrose prime test than males.	
Zhou et al. (2015)[10] *USA* Experiment 2	Sucrose reinforced operant conditioning	Rats Sprague-Dawley	21 M 18 F (sucrose experienced)	M&F	Adult	2 h	12h dark/ 12h light (lights off 0600)	IP OT 0.1, 0.3, 1.0, and 3.0mg/kg vs. vehicle (crossover design); injected 30 min before 4 conditioned cue or sucrose-primed reinstatement tests	Conditioned cue reinstatement test: active lever presses resulted in light/tone stimulus. Sucrose-primed reinstatement test: rats received one non-contingent pellet every 2 min for 10 min, and one pellet every 30 min thereafter, responding on either lever had no scheduled consequences. Food-restricted (~20g/day) to maintain 85% of ad lib BW.	Sucrose-conditioned cues - decreased active lever responding: females =0.1, 0.3, and 1 mg/kg OT (p<0.05); males =1 mg/kg (p<0.05), [sex × OT dose interaction, F(3,54)=2.93, p<0.05)]. Sucrose primed reinstatement - only affected by 1 mg/kg OT in males and females [F(3,51)=3.67, p<0.05]. OT no effect on inactive lever responding.	↓ cue-induced reward (F =0.1, 0.3, and 1.0; M =1mg/kg OT) ↓ sucrose seeking (1 mg/kg OT)
Ibragimov et al. (1988)[69] *Hungary* Experiment 2	Food-reinforced classical conditioning	Rats CFY albino	12/group	M	NR	6 d	12h light/ 12h dark (lights on 0600)	IP OT 150, 300, and 600mU/kg vs. saline; injection 20min before acquisition and extinction sessions.	Acquisition and extinction of conditioned feeding reflex (CFR) following 22 h food deprivation.	Acquisition of CFRs higher in treatment groups vs. control (NS). OT attenuated extinction of CFRs on days 3 (H=6.87, p=0.075) and 4 (H=6.82, p=0.089). Enhancement of total no. of CFRs not significant [F3,33=2.532, p=0.072). OT vs. control: 300mU/kg on day 3 (p<0.05) and 600mU/kg on day 4 (p<0.01.	↔

*Effect of exogenous oxytocin administration determined by alteration in dietary intake/behaviours [reported as increase (↑), decrease (↓) or neutral (↔)]. [a]Data represented graphically as mean ± SD or mean ± S.E.M; [b]Values reported as mean ± SD or mean ± S.E.M. Abbreviations: OT, oxytocin; ob/ob, rodent model of obesity due to mutations in the gene responsible for the production of leptin; NR, not reported; SC, subcutaneous; TGOT, [Thr4,Gly7]-OT (oxytocin analogue with longer half-life or higher oxytocin receptor specificity); LV, lateral ventricle; IP, intraperitoneal; ICV, intracerebroventricular; EIA, Enzyme Immunoassay; DIO, diet induced obesity; kcal, kilocalorie; AcbC, nucleus accumbens; db/db, diabetic & leptin-resistant rodent model; IV, intravenous; VMH, ventromedial hypothalamic nucleus; 3V, third ventricular; BLA, basolateral nuclei of the amygdala; CNA, central nuclei of the amygdala; ARC, arcuate nucleus; HFD, high fat diet; LFD, low fat diet; LBM, lean body mass, aCSF, artificial cerebrospinal fluid; RIA, radioimmunoassay; IO, intraoral; IV, intravenous; VTA, ventral tegmental area; BW, body weight; Na, sodium; EtOH, alcohol; NaCl, sodium chloride; NS, not significant; LiCL, lithium chloride.

Table 2. Descriptions and outcomes of included oxytocin receptor antagonist studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Baskin et al. (2010)[34] *USA*	Food intake	Rats Wistar	4-10/group	M	Adult	4 h (subset = 24 h)	12h light/ 12h dark, (lights off 1500)	3V ICV 10µg per 2µl OTr antagonist [d(CH2)Jyr(Me)-[Orn 8] OT vs. saline in rats treated with: OXY-SAP (cytotoxin, saporin conjugated to OT, to destroy cells that express OT receptors) vs. CON SAP (control, saporin conjugated to nonsense peptide). OT antagonist injected 35-45min before feeding.	Standard chow diet offered, after 6 h food deprivation, onset of dark cycle. Food intake measured (grams) at 0.5, 1, 2, 3, and 4 h during dark cycle, and cumulative food intake at 24 h. Water available ad lib.	In OXY-SAP normal stimulation of food intake following administration of OT antagonist (0.034 µg/µl) not observed ($p>0.05$). In CON-SAP + OT antagonist elevated food intake at 4 h by 77% ($p<0.01$). Mild increase in food intake in OXY-SAP (0.06 µg/µl) + saline compared with CON-SAP + saline over a 4-h period ($p=0.053$). Lower dose of OXY-SAP, no significant increase in food intake compared to CON-SAP ($p=0.16$).	↑
Herisson et al. (2016)[11] *NZ* Experiment 6	Food intake	Rats Sprague-Dawley	7/group	M	Adult	4 h	12h light/ 12h dark (lights on 0700)	2 nucleus accumbens core injections spaced 10 min apart: 1) saline + saline; 2) saline + 1 µg OT (lowest effective OT dose based on a previous exp.; 3) 0.3µl OTr antagonist (L-368,899) + 1µg OT; 4) 1µl L-368,899 + 1µg OT; or 5) 3µl L-368,899 + 1µg OT	Food intake (standard chow) measured (grams) at 2 and 4 h, following overnight food deprivation.	L-368,899 (OTr antagonist) counteracted the effect of OT at 2 h (3µg, $p=0.042$) and 4 h (1µg, $p=0.025$; 3µg, $p=0.016$).	↑ (compared to OT admin) ↔ (compared to saline controls)
Ho et al. (2014)[36] *USA* Experiment 2	Food intake	Rats Sprague-Dawley	7/group	M	Adult	30min	12h dark/ 12 h light (lights on 0100)	2 injections spaced 30min apart: 1) 4V vehicle or 10µg/2µL OTr antagonist, [d(CH2)51, Tyr(Me)2, Orn8]-OT, and 2) 4V vehicle or 1µg/1µL OT, crossover design. 2nd injection given 10 min before feeding.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at 30min.	Significant effect of treatment $F3,18=11.557$; $p<0.001$. 4V OT significantly reduced mean food intake vs. vehicle ($p=0.013$) or the OTr antagonist alone ($p=0.001$); effect fully blocked with prior admin. of OTr antagonist ($p=0.004$).	OT: ↓ OTr ant + OT: ↔

Ho et al. (2014)[36] *USA* Experiment 3	Food intake	Rats Sprague-Dawley	9/group	M	Adult	30 min	12h dark/ 12 h light (lights on 0100)	2 injections spaced 30min apart: 1) 4V vehicle or 10µg/2µL OTr antagonist, [d(CH2)51, Tyr(Me)2, Orn8]-OT, and 2) IP vehicle or 0.5 mg/kg OT, crossover design. 2nd injection given 10 min before feeding.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at 30min.	Food intake differed significantly between four groups F3,24=5.467; p=0.005. IP OT significantly reduced mean food intake vs. vehicle (p<0.05) or OTr antagonist alone (p<0.05). 4V OTr antagonist (same dose that blocked 4V OT in exp. 1) reversed anorectic effects of IP OT and responses did not differ significantly from vehicle (p>0.05).	OT: ↓ OTr ant + OT: ↔
Ho et al. (2014)[36] *USA* Experiment 4a & 4b	Food intake	Rats Sprague-Dawley	4a) 9/group 4b) 12/group	M	Adult	30min	12h dark/ 12 h light (lights on 0100)	Exp. a) 2 injections spaced 30min apart: 1) IP pre-treatment with 10µg/0.3 mL BBB penetrable OTr antagonist 9[d(CH2)51, Tyr(Me)2, Orn8]-OT and 2) IP vehicle or IP 0.5 mg/kg OT. Exp. b) 2 injections spaced 30min apart: 1) IP pre-treatment with 0.5 mg/kg non-penetrable OTr antagonist (D; L-371,257), and 2) IP vehicle or IP 0.5 mg/kg OT. 2nd injection given 10 min before feeding.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at 30min.	Exp. a) Food intake differed significantly between four groups F3,24=11.731; p<0.001. IP OT significantly reduced mean food intake vs. vehicle (p<0.05) or OTr antagonist alone (p<0.05). Pre-treatment with BBB penetrable OTr antagonist attenuated OT's effects by ~48%, resulting in food intake levels intermediate to those after vehicle or OT treatment (p<0.05). Exp. b) IP OT significantly reduced mean food intake vs. vehicle (p<0.05) or OTr antagonist alone (p<0.05). Pre-treatment with non-penetrable OTr antagonist attenuated OT's effects by ~67%, resulting in food intake levels intermediate to those after vehicle or OT treatment (pairwise comparison: p<0 .001; omnibus test: F3,33=12.867, p<0.001).	OT: ↓ OTr ant + OT: ↔

Ho et al. (2014)[36] *USA* Experiment 5	Food intake	Rats Sprague-Dawley	NR	M	Adult	30min	12h dark/ 12 h light (lights on 0100)	2 injections spaced 30min apart: 1) IP pre-treatment with 0.5 mg/kg non-penetrable OTr antagonist (D; L-371,257) or IP vehicle, and 2) 4V OT (2μg/1μL), crossover design.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at 30min.	4V OT inhibited food intake in presence (1.3±0.4 g) (IP L-371,257 + 4V OT) and absence of L-371,257 (1.4±0.6 g) (IP vehicle +4V OT) relative to vehicle treatment (4.46±0.6 g; p<0.01).	OT: ↓ OTr ant + OT: ↓
Ho et al. (2014)[36] *USA* Experiment 6	Food intake	Rats Sprague-Dawley	7-8/group	M	Adult	30min	12h dark/ 12 h light (lights on 0100)	IP OTr antagonist (L-371,257) 0.5 vs. 1.0 mg/kg vs. saline. Injection given 10min before feeding.	After 6-h fast, food (standard chow) given at onset of dark cycle. Food intake measured (grams) at 30min.	L-371,257 (1mg/kg) increased food intake at 30 minutes (p=0.082) and 0.5mg/kg at 3 h (p=0.092). L-371,257 (0.5mg/kg) stimulated food intake vs. vehicle by 4 hours (p<0.05).	↑
Huang et al. (1996)[92] *Iceland*	Food intake/dehydration	Rats Lewis x DA F1 hybrids	8 dehydrated-vehicle (DH-veh) 8 dehydrated-antagonist (DH-ant) 9 Control	M	Adult	5 d	NR	SC infusion via mini-pump: 40μg/h^{-1}/kg BW^{-1} OT antagonist [1-(3-mercaptopropionic acid),2-0-ethyl-D-Tyr,4-Thr,8_Orn]-OT vs. saline; infusion period =days 3-5. Plasma OT via RIA.	Food intake (standard chow) measured (g/day): day 1-2 baseline intake; day 3-4 intake pre-24 h water deprivation; day 5 intake during 24 h water deprivation (dehydration groups: no access to water; Control group: free access to water).	Day 1-2: food intake similar between groups; day 3-4: DH-ant and DH-veh reduced food intake (NS); day 5: Dehydration caused ~30% decrease in food intake in all groups (p<0.01). Plasma OT in DH-veh increased from 15.5±1.2[a] to 23.8±2.0[a] pg/mL (p<0.01) at end of 24 h dehydration. Plasma OT in DH-ant not reported.	↑
Klockars et al. (2017a)[73] *NZ & USA* Experiment 2	Food intake	Rats Sprague-Dawley	8/group,	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	2 IV injections (15–20min apart) prior to intake testing, 4 conditions: 1) saline + saline (control); vs. 2) saline + 0.3μg/kg OT; vs 3) 30μg/kg OTr antagonist ([d(CH2)51, Tyr(Me)2, Orn8]-OT) + 0.3μg/kg OT; vs. 4) 30μg/kg OTr antagonist + saline.	Following overnight food deprivation, food intake (standard chow, 3.6kcal/g) measured (grams) 2 h post-injection. Water available ad lib.	Hypophagia induced by IV OT was reversed by a pre-treatment with OTr antagonist (p>0.05).	OT: ↓ OTr ant + OT: ↔
Klockars et al. (2017b)[75] *NZ & USA* Experiment 2	Food intake	Rats Sprague-Dawley	6-7/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VHM 1.0μg and 3.0μg Otr antagonist (L-368,899)vs. saline; injected just before testing.	Following overnight food deprivation, food intake (standard chow) measured (grams) 1 h and 2 h post-injection.	3.0μg OTr antagonist did not increase chow intake after overnight deprivation (p>0.05).	↔

Klockars et al. (2017b)[75] *NZ & USA* Experiment 3	Food intake	Rats Sprague-Dawley	6/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	2 IV injections (15min apart) prior to intake testing, 3 conditions: 1) saline + saline (control); vs. 2) saline + 1.0µg OT; vs 3) 1.0µg OTr antagonist (L-368,899) + 1.0µg OT. 2nd injection given 5-10min before feeding.	Following overnight food deprivation, food intake (standard chow) measured (grams) 1 h and 2 h post-injection.	Effect of 1.0µg VHM OT on hunger-driven feeding (p=0.0027) was reversed by a pre-treatment with 1.0µg OTr antagonist (p>0.05).	OT: ↓ OTr ant + OT: ↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 7	Food intake	Rats Sprague-Dawley	9/group	M	Adult	4 h	12h light/ 12h dark cycle (lights on 0700)	2 BLA injections (10min apart) prior to intake testing, 4 conditions: 1) saline + saline (control); vs. 2) saline + 1.0µg OT; vs 3) 1.0µl OTr antagonist (L-368,899) + 1.0µg/kg OT; vs. 4) 1.0µl Otr anatagonist + saline.	Following overnight food deprivation, food intake (standard chow) measured (grams) 4 h post-injection.	BLA OT 1µg significantly reduced intake of chow [F(3, 32)=2.514, p=0.0323]. OTr attenuated OT effects (NS).	OT: ↓ OTr ant + OT: ↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 8	Food intake	Rats Sprague-Dawley	9/group	M	Adult	4 h	12h light/ 12h dark cycle (lights on 0700)	2 CNA injections (10min apart) prior to intake testing, 4 conditions: 1) saline + saline (control); vs. 2) saline + 1.0µg OT; vs 3) 1.0µl OTr antagonist (L-368,899) + 1.0µg/kg OT; vs. 4) 1.0µl Otr anatagonist + saline.	Following overnight food deprivation, food intake (standard chow) measured (grams) 4 h post-injection.	CNA OT 1µg significantly reduced intake of chow [F(3, 32)=3.13, P=0.0484]. OTr attenuated OT effects (NS).	OT: ↓ OTr ant + OT: ↔
Olson et al. (1991b)[76] *USA*	Food intake	Rats Sprague-Dawley	10 treatment 41 vehicle	M	Adult	90min	12h light/ 12h dark (lights on 0700)	2 ICV LV injections 15 and 30 min prior intake testing. Drug conditions: 9nmol OTr antagonist [d(CH2)51, Tyr(Me)2, Orn8]-OT) + vehicle (aCSF) vs. vehicle + vehicle.	Food intake measured (grams) at 15, 30, 60 and 90min. 22 h food deprivation prior to testing. Food (standard chow) and water available ad lib.	Baseline food intakes prior to testing comparable to vehicle + vehicle group. Treatment with vehicle + OTr antagonist did not increase food intake significantly (p<0.05).	↔
Olson et al. (1991a)[70] *USA* Experiment 2	Food intake	Rats Sprague-Dawley	4 (0.8nmol dose) 4 (8nmol dose) 5 (20nmol dose)	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	ICV LV OT antagonist - [(CH2)51,Phe(Me)2,Thr 4,Orn8]OT: 0.8nmol or 8nmol or 20nmol vs. vehicle (aCSF), within subject design; injected 45 min before feeding	Following 16 h fast, ad lib access to food. Food intake measured (grams) at 1 h.	Doses of 0.8 or 8 nmol did not increase deprivation-induced feeding (p>0.05). Dose 20 nmol inhibited food intake (p<0.05). Partial agonist effects at high doses [F(3,24)=4.2, p<0.02]	↔ (0.8 & 8 nmol) ↓ (20nmol)

Olson et al. (1991a)[70] *USA* Experiment 3	Food intake	Rats Sprague-Dawley	6 (4nmol dose OT) 5 (10nmol dose OT)	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	2 ICV LV injections: 1) Pre-treatment with 8nmol OT antagonist - [(CH2)51,Phe(Me)2,Thr 4,Orn8]OT, and 15 min later 2) OT 4 or 10nmol, vs. vehicle (aCSF), within subject design.	Following 16 h fast, ad lib access to food. Food intake measured (grams) at 1 h.	Pre-treatment with OT antagonist completely blocked inhibitory effects on food intake produced by OT 4nmol ($p<0.05$) and 10 nmol ($p<0.001$).	↓ (OT) OTr ant + OT: ↔
Olszewski et al. (2010)[48] *Sweden* Experiment 1	Food intake	Mice C57BL/6J	9/group (sated)	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist - L368,899: 0.3 or 1.0 or 3.0mg/kg vs. saline; injected just before feeding.	Ad lib access to chow, intake measured (grams) at 2h.	No difference in food intake between groups ($p<0.05$).	↔
Rinaman et al. (2002)[44] *USA*	Food intake	Rats Sprague-Dawley	6-10/group	M	NR	4 h	12h light/ 12h dark (lights on 0700)	ICV LV infusions - 5 conditions (crossover design): 1) no infusion; 2) vehicle (saline); 3) 1µg OT; 4) OT blocker [d(CH2)5, Tyr(Me)2, Orn8]vasotocin; and 5) OT blocker/1µg OT, given 5 min apart; injections given just before feeding.	Following 20 h fast, ad lib access to food at lights out. Cumulative 4 h intake measured (grams, expressed as percent BW).	Food intake significantly inhibited only after infusion of OT ($p<0.05$ with each other treatment)	↓ (OT) ↔ (vehicle, OT blocker and OT blocker/OT)
Uchoa et al. (2009)[42] *Brazil* Experiment 1	Food intake	Rats Wistar	5-6/group	M	NR	1 h	12h light/ 12h dark (lights on 0600)	ICV LV OTr antagonist – 5µg/5µl [d(CH2)5,Tyr(Me)2, Orn8]-vasotocin vs. vehicle (saline); injected 15 min before feeding.	Following 16 h fast, ad lib access to food. Intake measured (g/100g) at 1 h.	No significant difference in food intake between groups ($p>0.05$).	↔
Uvnas-Moberg et al. (1996)[62] *Sweden* Experiment 2	Food intake	Rats Sprague-Dawley (SGR = slowly growing rats)	35 Test conditions: 1) 5/group 2) 5/group 3) 10/group 4) 5/group 5) 5/group 6) 5/group	F	10 wk	1-4 d	12h light/ 12h dark (lights on 0600)	Daily SC injection, 6 test conditions: 1) vehicle (saline) for 4 days; 2) 0.1mg/kg OT for 4 days; 3) 1mg/kg OT for 4 days; 4) 1.5 mg/kg OT antagonist (1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin) for 4 days; 5) 1.5mg/kg OT antagonist + 1.0mg/kg OT for 4 days; 6) 1.0 mg/kg OT for 1 day and vehicle for 3 days. Injected at 1800 (onset of dark period when rats feed). Baseline plasma OT measured via RIA =31.2±13.6 pmol/L.	Ad lib access to food and water, intake measured (grams) daily.	No significant differences in food intake between groups ($p>0.05$)	↔

Zhang et al. (2011)[45] *USA* Experiment 3	Food intake		5-7/group normal weight	M	Adult	1 wk	12h light/ 12h dark	Daily IP 1mg/kg OTr antagonist [D-(CH2)5,Tyr(Me)2,Orn8] vasotocin (OVT) vs. saline; injected start of daytime (AM).	Ad lib access to standard chow diet. Weekly daytime, nighttime and total food intake (kcal), and diurnal ratio (daytime caloric intake divided by nighttime caloric intake) measured.	OTr antagonist vs. saline significantly increased daytime food intake ($p<0.05$), but not nighttime. Ratio of daytime to nighttime food intake significantly elevated ($p<0.05$).	↑ AM food intake ↑ diurnal ratio
Zhang et al. (2011)[45] *USA* Experiment 4	Food intake	Mice C57BL/6	4-9/group normal weight	M	Adult	1 wk	12h light/ 12h dark	ICV 3V 4µg OTr antagonist [D-(CH2)5,Tyr(Me)2,Orn8] vasotocin (OVT)] vs. vehicle (aCSF); injected at the beginning of daytime (AM) vs. nighttime (PM).	Ad lib access to standard chow diet. Weekly daytime, nighttime and total food intake (kcal), and diurnal ratio (daytime caloric intake divided by nighttime caloric intake) measured.	OTr antagonist (day and nighttime injections) vs. saline significantly increased total weekly food intake ($p<0.05$), slightly elevated by daytime vs. nighttime treatment ($p<0.05$). Diurnal ratio (daytime: nighttime feeding) increased significantly by AM ($p<0.05$), but not PM treatment ($p>0.05$).	↑ food intake ↑ diurnal ratio (AM OT admin)
Lokrantz et al. (1997)[64] *Sweden* Experiment 2	Glucose intake	Rats Sprague-Dawley	8 non-deprived	M	NR	Test 1: until satiety criterion met; Test 2: 60 min after end of 1st test	12h light/ 12h dark	3 ICV LV injection conditions: 20 nmol OT vs. 20 nmol Otr antagonist [(1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-OT] vs. vehicle (saline). Injections 30min prior to 1st intake test and 45min prior to 2nd intake test.	Test 1 and 2: 12.5% glucose (wv) delivered intraorally via peristaltic pump rate of 1.0 ml/min till satiety reached. Total intake measured (mL).	Total session intake: overall condition effect was significant [$F(2,14)=21.12$, $p<0.0001$], significantly higher intake for the OTr ant ($p<0.0001$) condition. OT had no effect.	OT: ↔ OT ant: ↑
Lokrantz et al. (1997)[64] *Sweden* Experiment 3	Glucose intake	Rats Sprague-Dawley	8 food deprived	M	NR	IO glucose infusion until satiety criterion met	12h light/ 12h dark	2 ICV LV injections OTr antagonist, 1-deamino-2-D-Tyr- (OEt) -4-Thr-8-Orn-OT, 45 and 30 min prior intake testing. Drug conditions: Vehicle (saline) + OT (20 nmol), OTr antagonist (20 nmol) + vehicle, OTr antagonist (20 nmol) + OT (20 nmol), or vehicle + vehicle.	12.5% glucose (wv) delivered intraorally via peristaltic pump rate of 1.0 ml/min. Total intake measured (mL). 20 h food deprivation prior to testing.	1st-test intake: significant overall effect of injection condition on first-meal intake [$F(3,21)=31.29$, $p<0.0001$]. OT (20 nmol) significantly (45%) lowered intake vs. vehicle ($p<0.0001$). 2nd-test intake: decline in first-test intake under OT offset by second-test intake increase, no difference in intakes between OT and vehicle, OTr ant. and vehicle. Significant increase in	OT: ↔ OTr ant: ↑ OTr ant + OT: ↔

										total session intake for OTr ant. vs. vehicle ($p<0.0001$). OT + OTr ant. No significant intake effects vs vehicle.	
Klockars et al. (2017a)[73] *NZ & USA* Experiment 9	Sucrose intake	Rats Sprague-Dawley	6/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV 30µg/kg OTr antagonist ([d(CH2)51, Tyr(Me)2, Orn8]-OT) vs. saline; injected prior to testing.	Intake of 10% sucrose solution measured (grams) 2 h post-injection; no access to chow or water.	Hypophagia induced by IV OT was reversed by a pre-treatment with Otr antagonist ($p>0.05$).	OT: ↓ OTr ant + OT: ↔
Klockars et al. (2017b)[75] *NZ & USA* Experiment 7	Sucrose intake	Rats Sprague-Dawley	11/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VHM 1.0µg OTr antagonist (L-368,899) vs. saline; injected prior to testing.	Intake of 10% sucrose solution measured (grams) 1 h and 2 h post-injection; no access to chow or water.	2h consumption of sucrose remained unchanged after OTr anatagonist 1.0µg ($p>0.05$).	↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 9	Sucrose intake	Rats Sprague-Dawley	9/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	2 BLA injections (10min apart) prior to intake testing, 4 conditions: 1) saline + saline (control); vs. 2) saline + 1.0µg OT; vs 3) 1.0µl OTr antagonist (L-368,899) + 1.0µg/kg OT; vs. 4) 1.0µl OTr anatagonist + saline.	Intake of 10% sucrose solution measured (grams) 2 h post-injection; no access to chow or water.	BLA OT 1µg significantly reduced intake of sucrose [$F(3, 32)=2.446$, $p=0.033$]. OTr attenuated OT effects (NS).	OT: ↓ OTr ant + OT: ↔
Mullis et al. (2013)[71] *USA* Experiment 2	Sucrose intake	Rats Wistar	6 naïve	M	NR	30 min	12h light/ 12h dark	Intra-VTA OTr antagonist: 0.1, 3 or 10µg d(CH2)51,Tyr(Me)2,Orn8)-vasotocin vs. saline (crossover design); injection 15 min before testing	Intake of 10% sucrose solution measured (grams); no access to food or water	OTr antagonist significantly increased sucrose intake by ~17-20.5% [$F(3,15)=4.58$, $p< 0.05$] at all doses vs. saline (all $p< 0.05$)	↑
Mullis et al. (2013)[71] *USA* Experiment 3	Sucrose intake	Rats Wistar	8 naïve	M	NR	30 min	12h light/ 12h dark	Intra-VTA non-peptide OTr antagonist: 1 or 5µg L-368,899 vs. saline (crossover design); injection 15 min before testing	Intake of 10% sucrose solution measured; no access to food or water	OTr antagonist significantly increased sucrose intake by ~17-20.5% [$F(2,14)=4.88$, $p < 0.05$], with 5µg OT dose differing significantly from vehicle ($p<0.01$) and 1µg dose not significant ($p=0.054$).	↑ (5µg OT) ↔ (1µg OT)
Mullis et al. (2013)[71] *USA* Experiment 4	Sucrose intake	Rats Wistar	7 naïve	M	NR	30 min	12h light/ 12h dark	2 VTA injections 30 and 15 min before testing: 1) 0.5µg OTr antagonist (L-368,899) or vehicle (saline) 2) 1µg OT or vehicle	Intake of 10% sucrose solution measured (grams); no access to food or water	Significant main effect of OT [$F(1,6)=14.16$, $p<0.01$] and interaction between L-368,899 and OT [$F(1,6)=12.81$, $p< 0.05$].	↓ (OTr + OT) ↓ (vehicle + OT)

										VTA OT significantly suppressed sucrose intake whether or not rats pre-treated with L-368,899 (all p<0.01). OT effect significantly smaller after L-368,899 pre-treatment (16%) relative to vehicle pre-treatment (28%) (p < 0.01). Sucrose intake after L-368,899 + OT significantly higher than vehicle + OT (p < 0.05).	↑ (OTr + vehicle)
Olszewski et al. (2010)[48] *Sweden* Experiment 2	Sucrose intake	Mice C57BL/6J	9/group (sucrose experienced)	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist - L368,899: 0.3 or 1.0 or 3.0mg/kg vs. saline; injected just before feeding.	Ad lib access to 10% sucrose solution from 1500-1700 h, intake measured (mL) at 2 h. Chow and water unavailable.	OT antagonist 1mg/kg BW (p=0.063) and 3mg/kg BW (p=0.031) increased intake of sugar.	↔ (0.3mg/kg) ↑ (1 and 3mg/kg)
Herisson et al. (2014)[35] *NZ* Experiment 1	CHO vs. non-CHO (saccharin) intake	Mice C57BL/6J	8/group "sucrose and saccharin experienced"	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist L-368,899 0.1, 0.3, 1 and 3mg/kg BW. vs. saline; injected 5min before feeding.	No-choice single-bottle paradigm: solutions containing either 10% sucrose, 30% sucrose, 10% fructose, 10% glucose, 10% polycose, 0.1% saccharin or 10% cornstarch suspension. Access after overnight food deprivation. Amounts ingested recorded (g/kg BW). Food and water unavailable during testing.	OTr antagonist increased intake of all CHO. Sucrose intake (L-368,899 dose mg/kg BW): 10% sucrose (0.3mg/kg) p=0.025, (1mg/kg) p=0.008; 30% sucrose (0.3mg/kg) p=0.012, (1mg/kg) p=0.027. Fructose, glucose, polycose and cornstarch intakes increased, lowest effective dose of L-368,899 was 3mg/kg (fructose: p=0.016; glucose: p=0.020; polycose: p=0.031; cornstarch: p=0.039). Non-significant effect on saccharin at 3mg/kg (p=0.088).	↑
Herisson et al. (2014)[35] *NZ* Experiment 2	CHO vs. non-CHO (saccharin) intake	Mice C57BL/6J	6/group "sucrose and saccharin experienced"	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist L-368,899 0.1mg/kg BW vs. saline; injected 5min before feeding.	Two-bottle choice test: sugar (10% sucrose, glucose or fructose) vs. 0.1% saccharin. Amounts ingested recorded (g/kg BW). Food and water	Sucrose intake doubled vs. saccharin intake (p=0.006). No effect on preference for fructose or glucose vs. saccharin.	↑

									unavailable during testing.		
Herisson et al. (2016)[11] *NZ* Experiment 7	Sucrose and saccharin intake	Rats Sprague-Dawley	7-8/group	M	Adult	2 h	12h light/ 12h dark (lights on 0700)	2 nucleus accumbens core injections spaced 10 min apart: Sucrose tests - 1) saline + saline; 2) saline + 0.3 µg OT; or 3) 1µl OTr antagonist (L-368,899) + 0.3µg OT. Saccharin tests - 1) saline + saline; 2) saline + 0.03 µg OT; or 3) 3µl OTr antagonist (L-368,899) + 0.03µg OT.	Intake (grams) of 10% sucrose solution vs. 0.1% saccharin. Food and water unavailable.	L-368,899 (OTr antagonist) abolished effect of OT on intakes of sucrose (p=0.030) and saccharin (p=0.04) solutions.	↑ (compared to OT admin) ↔ (compared to saline controls)
Klockars et al. (2017a)[73] *NZ & USA* Experiment 10	Saccharin intake	Rats Sprague-Dawley	6/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV 30µg/kg OTr antagonist ([d(CH2)51, Tyr(Me)2, Orn8]-OT) vs. saline; injected prior to testing.	Intake of 0.1% saccharin solution measured (grams) 2 h post-injection; no access to chow or water.	Hypophagia induced by IV OT was reversed by a pre-treatment with OTr antagonist (p>0.05).	OT: ↓ OTr ant + OT: ↔
Klockars et al. (2017b)[75] *NZ & USA* Experiment 8	Saccharin intake	Rats Sprague-Dawley	6/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	VHM 1.0µg OTr antagonist (L-368,899) vs. saline; injected prior to testing.	Intake of 0.1% saccharin solution measured (grams) 1 h and 2 h post-injection; no access to chow or water.	2h consumption of saccharin remained unchanged after OTr anatagonist 1.0µg (p>0.05).	↔
Klockars et al. (2018)[74] *NZ & USA* Experiment 10	Saccaharin intake	Rats Sprague-Dawley	9/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	2 BLA injections (10min apart) prior to intake testing, 4 conditions: 1) saline + saline (control); vs. 2) saline + 1.0µg OT; vs 3) 1.0µl OTr antagonist (L-368,899) + 1.0µg/kg OT; vs. 4) 1.0µl Otr anatagonist + saline.	Intake of 0.1% saccharin solution measured (grams) 2 h post-injection; no access to chow or water.	BLA OT 1µg significantly reduced intake of saccharin [F(3, 32)=4.443, p=0.0219]. OTr attenuated OT effects (NS).	OT: ↓ OTr ant + OT: ↔
Olszewski et al. (2010)[48] *Sweden* Experiment 3	Sucrose vs. fat intake	Mice C57BL/6J	NR	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist - L368,899: 0.3 or 1.0 or 3.0mg/kg vs. saline; injected just before feeding.	Ad lib concurrent access to 10% sucrose solution and Intralipid solution* from 1500-1700 h, intake measured (mL) at 2 h. Chow and water unavailable.	OT antagonist 1 mg/kg BW preferentially increased intake of sugar [sugar = ~67% of total intake, interrupted from graph] (p=0.019) without affecting total amount of ingested energy, 0.3-mg/kg BW dose produced	↑ (1mg/kg - sucrose) ↔ (0.3mg/kg - sucrose) ↔ (0.3 and

										no change in sucrose intake (p>0.05).	1mg/kg - fat)
Olszewski et al. (2010)[48] *Sweden* Experiment 4	Palatable high fat intake	Mice C57BL/6J	9/group (fat experienced)	M	NR	2 h	12h light/ 12h dark (lights on 0700)	IP OTr antagonist - L368,899: 0.3 or 1.0 or 3.0mg/kg vs. saline; injected just before feeding.	Ad lib access to Intralipid solution from 1500-1700 h, intake measured (mL) at 2h. Chow and water unavailable.	OT antagonist had no effect on Intralipid consumption (p>0.05).	↔
Klockars et al. (2017a)[73] *NZ & USA* Experiment 11	Palatable high fat intake	Rats Sprague-Dawley	6/group	M	Adult	2 h	12h light/ 12h dark cycle (lights on 0700)	IV 30µg/kg OTr antagonist ([d(CH2)51, Tyr(Me)2, Orn8]-OT) vs. saline; injected prior to testing.	Intake of 4.1% Intralipid emulsion measured (grams) 2 h post-injection; no access to chow or water.	Hypophagia induced by IV OT was reversed by a pre-treatment with OTr antagonist (p>0.05).	OT: ↓ OTr ant + OT: ↔
King et al. (2017)[12] *USA* Experiment 4	Alcohol intake	Mice C57BL/6J	40 (10/group)	M	9-10 wk	24 h	Reversed 12h light/ 12h dark cycle	2 IP injections: 1) Pre-treatment with 10 mg/kg OTr antagonist - L-368,899 or vehicle (saline), and 15 min later 2) OT 1.0mg/kg or vehicle (saline)	Days 1-3: daily 2 h access to single 15mL bottle of 20% (v/v) EtOH 3h into dark phase. Day 4: access to EtOH for 4 h.	OT 1.0 mg/kg reduced EtOH intake vs vehicle ($p < 0.001$) and this effect was reversed by pre-treatment with OTr anatagonist; OT x OTr antagonist interaction, $F(1, 36) = 10.36$; $p<0.003$. OTr anatagonist did not alter EtOH intake when given alone.	OT: ↓ OTr ant + OT: ↔
Arletti et al. (1989)[13] *Italy* Experiment 6	Feeding behaviour	Rat Sprague-Dawley	28 (7/group)	M	NR	1 h	Natural light-dark cycle	4 test conditions: 1) Pre-treatment of ICV LV OTr antagonist - [d(CH2)Jyr(Me)-[Orn 8] vasotocin 10 µg/rat 15min before treatment of ICV LV OT 10 µg/rat vs. 2) pre-treatment of ICV LV OT antagonist 10 µg/rat, injected 15min before ICV LV saline 5µl vs. 3) pre-treatment ICV LV saline 5µl 15min before treatment of ICV LV OT 10 µg/rat vs. 4) pre-treatment ICV LV saline 5µl 15min before treatment of ICV LV saline 5µl.	Food intake (grams of standard chow), latency to 1st meal (sec), meal duration (sec) and no. of meals, following 21h fast.	Pre-treatment with OT antagonist 15 min before OT injection antagonized all effects of OT. OT antagonist significantly increased duration of feeding, amount of food consumed and decreased latency to first meal compared to saline-treated rats.	OTr ant + OT: ↔
Arletti et al. (1990)[14] *Italy* Experiment 7	Feeding behaviour	Rat Sprague-Dawley	ICV treatment ≥7/group	M	NR	1 h	Natural light-dark cycle	4 test conditions: 1) ICV LV OT 10µg/rat vs. 2) ICV LV OTr antagonist - [d(CH2)Jyr(Me)-[Orn 8]	Food intake (grams of standard chow), latency to 1st meal (sec), meal	ICV OT 10µg/rat significant reduction in food intake, time spent eating and increased the	OTr ant + OT: ↔ OT ant: ↑

								vasotocin 10µg/rat vs. 3) Pre-treatment of ICV LV OT antagonist 10 µg/rat 15min before treatment of ICV LV OT 10 µg/rat vs. 4) saline. Injected just before feeding.	duration (sec) and no. of meals, following 21h fast.	latency to 1st meal ($p<0.05$); number of meals not modified. Pre-treatment with OT antagonist + equal dose of OT completely prevented effect of OT. OT antagonist increased food intake and time spent eating, and reduced the latency to the first meal. Food intake: $F(3,21)=36.72$, $p<0.00001$; latency to 1st meal: $F(3,21)=37.61$, $p<0.00001$; feeding time: $F(3,21)=30.35$, $p<0.00001$.	
Olszewski et al. (2014)[39] *NZ* Experiment 1	Sucrose intake in moderately novel environment	Mice BALB/c	14 tastant experienced (condensed milk or 0.1% saccharin) 14 tastant naïve	M	NR	35min (5 min pair interaction; 30min feeding)	12h light/ 12h dark (lights on 0600)	IP OTr antagonist (L-368,899) 10mg/kg BW vs. saline; tastant naïve mice injected 5 min prior to interaction with tastant experienced mice.	Following overnight fast, in moderately novel environment (freshly changed cage) tastant naive mice allowed to interact with tastant experienced mice for 5 min before testing (i.e. 2/cage). Tastant naive mice given ad lib access to sweetened condensed milk (diluted in water 1:3), latency to begin consumption (sec) and amount of food eaten measured (g/g BW); no access to food or water during testing.	L-368,899 reduced effect of social transmission of preference for novel tastant (condensed milk) via exposure of tastant exposed mice to conspecifics that have just consumed this tastant ($p<0.05$). No effect when conspecifics were exposed to saccharin instead of milk ($p>0.05$).	↓
Olszewski et al. (2014)[39] *NZ* Experiment 2	Sucrose intake in highly novel environment	Mice BALB/c	14 tastant experienced (condensed milk) 25 tastant naïve	M	NR	15 min	12h light/ 12h dark (lights on 0600)	IP OTr antagonist (L-368,899) 10mg/kg BW vs. saline; tastant naïve mice injected 10 min prior to interaction with tastant experienced mice.	Following overnight fast, in highly novel environment (brightly lit arena) tastant naive mice allowed to interact with tastant experienced mice for 5 min before testing (i.e. 2/cage). Tastant naive mice given ad lib access to sweetened condensed milk (diluted in water 1:3), latency to	Pre-treatment with L-368,899 reduced effect of social transmission of preference for novel tastant (condensed milk) via exposure of tastant exposed mice to conspecifics that had just consumed tastant ($p<0.05$).	↓

									begin consumption (sec) and amount of food eaten (g/g BW) measured (11:00-11:30); no access to food or water during testing.		
Olszewski et al. (2015)[61] *NZ* Experiment 1	Sucrose intake in non-social vs social setting	Mice C57BL/6N	9 dyads (1 dominant + 1 subordinate) per each drug treatment condition	M	9 wk	10 min	12h light/ 12h dark (lights on 0700)	IP OTr antagonist (L-368,899) 0.3, 1.0.0 or 3 mg/kg vs. saline; injected 5-10 min before testing.	Following overnight fast, 4 social context paradigms: 1) no social exposure = mice from each dyad placed individually in apparatus with access to 10% sucrose solution; 2) olfactory-derived social exposure, mice from each dyad placed individually in apparatus (containing soiled bedding from respective dyad's home cage) with access to 10% sucrose solution; 3) partial social exposure, both mice from each dyad placed in apparatus simultaneously in separate compartments with access to 10% sucrose solution (one mouse received antagonist and one saline); and 4) full social exposure = both mice from each dyad placed in same compartment of apparatus, shared access to single 10% sucrose solution (mL/g BW), % time spent drinking (%) calculated. Paradigms 1–3 sucrose intake measured. Testing 0900 to 1130.	Dominant mice - OTr antagonist (0.3 and 1mg) increased amount of sugar consumed in non-social (saline vs 0.3 mg/kg: p=0.040; saline vs 1 mg/kg: p=0.047), olfactory-derived (saline versus 0.3 mg/kg: p=0.031; saline vs 1 mg/kg: p=0.045) and partial social exposure paradigm (saline vs 0.3 mg/kg: p=0.009; saline vs 1 mg/kg: p=0.029); increased amount of time spent drinking sweet solution in full social exposure paradigm (saline vs 0.3 mg/kg: p=0.006; saline vs 1 mg/kg: p=0.018). Subordinate mice - OTr antagonist (0.3 and 1mg) increased amount of sugar consumed in non-social paradigm only (saline vs 0.3 mg/kg: P = 0.038; saline vs 1 mg/kg: p=0.020).	↑ intake and time spent feeding in social and non-social context (dominant mice) ↑ intake and time spent feeding in non-social context (subordinate mice)

*Effect of oxytocin receptor antagonist administration determined by alteration in dietary intake/behaviours [reported as increase (↑), decrease (↓) or neutral (↔)]. [a]mean±SE. Abbreviations: OT, oxytocin; 3V, third ventricular; ICV, intracerebroventricular; OTr, oxytocin receptor; 4V, fourth ventricular; OTr ant, oxytocin receptor antagonist; IP, intraperitoneal; NR, not reported; BBB, blood–brain barrier; BW, body weight; RIA, radioimmunoassay; NS, not significant; SC, subcutaneous; IV, intravenous; VHM, ventromedial hypothalamic nucleus; BLA, basolateral nuclei of the amygdala; CNA, central nuclei of the amygdala; LV, lateral ventricle; aCSF, artificial cerebrospinal fluid; IO, intraoral; VTA, ventral tegmental area; CHO, carbohydrate; non-CHO, non-carbohyrate; EtOH, alcohol.

Table 3. Description and outcomes of oxytocin agonist studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Olson et al. (1991a)[70] *USA* Experiment 4	Food intake	Rats Sprague-Dawley	4 (10pmol dose) 4 (25pmol dose) 12 (50pmol dose) 9 (500pmol dose)	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	ICV LV OT agonist - [e-L-β-MePhe2]OT: 10pmol or 25pmol or 50pmol or 500pmol vs. vehicle (aCSF), within subject design; injected just before feeding	Following 16 h fast, ad lib access to food. Food intake measured (grams) at 1 h.	OT agonist significantly decreased food intake at doses of 10, 25, 50 and 500 pmol $F(4,36)=9.42$, $p<0.001$; similar inhibition of food intake for all doses vs. saline, all $p<0.05$.	↓
Olson et al. (1991a)[70] *USA* Experiment 5	Food intake	Rats Sprague-Dawley	7	M	Adult	3 d	12h light/ 12h dark (lights on 0700)	Daily injection of ICV LV OT agonist - [e-L-β-MePhe2]OT: 100pmol vs. vehicle (aCSF), within subject design; injected 30 min before feeding	Following 16 h fast, ad lib access to food. Food intake measured (grams) at 1 h.	OT agonist vs. vehicle decreased food intake on day 1 ($p<0.001$) and day 2 ($p<0.05$). Day 3 intake not significantly different from baseline i.e. development of tolerance to agonist's inhibitory effects on food intake. Overall, 3-day intake: $[F(3,18)=22.4, p<0.001]$.	↓
Olson et al. (1991a)[70] *USA* Experiment 6	Food intake	Rats Sprague-Dawley	5	M	Adult	3 d	12h light/ 12h dark (lights on 0700)	Day 1-3, combined treatment of two daily ICV LV injections: 1) Pre-treatment with 8nmol OTr antagonist - [(CH2)51,Phe(Me)2,Thr 4,Orn8]OT 45 min before feeding, and 15 min later 2) OT agonist - [e-L-β-MePhe2]OT: 50pmol (day 1), 100pmol (day 2) or 500pmol (day 3), vs. vehicle (aCSF), within subject design. Day 4: single treatment of 100pmol OT agonist - [e-L-β-MePhe2]OT vs. vehicle (aCSF), within subject design.	Following 16 h fast, ad lib access to food. Food intake measured (grams) at 1 h.	Increasing doses of OT agonist over 3 days had no effect on food intake when pre-treated with OTr antagonist. Day 4, OT agonist (without OTr antagonist pre-treatment) inhibited food intake to 66±6% of baseline values $[F(4,16)=9.65, p<0.001]$.	↔ (antagonist + agonist) ↓ (agonist)

Olson et al. (1991a)[70] *USA* Experiment 7	Time spent feeding	Rats Sprague-Dawley	7 treatment 9 vehicle	M	Adult	1 h	12h light/ 12h dark (lights on 0700)	ICV 100pmol OT agonist - [e-L-β-MePhe2]OT vs. vehicle (aCSF), injected just before feeding.	Following 16 h fast, ad lib access to food. Time spent holding and chewing food measured over 1 h. Distribution of food intake (grams) also measured as sequential 10 min blocks.	OT agonist produced significant decrease in time spent feeding vs. vehicle ($p<0.001$). Distribution of food intake during 6x 10 min intervals similar for both groups ($p>0.05$).	↓
Olszewski et al. (2014)[39] *NZ* Experiment 3	Sugar intake in highly novel environment	Mice BALB/c	7-8/group (tastant experienced)	M	NR	10 min	12h light/ 12h dark (lights on 0600)	IP OT agonist (WAY-267,464) 3, 10 or 30mg/kg BW vs. saline; injected 5 min prior to feeding (11:00).	Highly novel environment (brightly lit arena): access to sweetened condensed milk (diluted in water 1:3), latency to begin consumption (sec) measured; no access to food or water during testing.	WAY-267,464 (10 and 30mg doses only) diminished latency to approach food and increased amount of food eaten in anxiety provoking conditions ($p<0.05$).	↑ intake, ↓ latency (10 and 30mg/kg)
Olszewski et al. (2014)[39] *NZ* Experiment 4	Sugar intake in moderately novel environment	Mice BALB/c	7-9/group (tastant experienced)	M	NR	1 h	12h light/ 12h dark (lights on 0600)	IP OT agonist (WAY-267,464) 3, 10 or 30mg/kg BW vs. saline; injected 5 min prior to feeding (11:00-11:30).	Following 20 h fast, moderately novel environment (freshly changed cage): ad lib access to sweetened condensed milk (diluted in water 1:3), latency to begin consumption (sec) and amount of food eaten (g/g BW) measured; no access to food or water during testing.	WAY-267,464 (10 and 30mg doses only) diminished latency to approach food and increased amount of food eaten in anxiety provoking conditions ($p<0.05$).	↑ intake, ↓ latency (10 and 30mg/kg)
Olszewski et al. (2014)[39] *NZ* Experiment 5	Sugar intake in highly novel environment	Mice BALB/c	8-9/group (tastant experienced)	M	NR	10 min	12h light/ 12h dark (lights on 0600)	2 IP injections (5 min apart) prior intake testing, 4 conditions: 1) saline + saline (controls); vs. 2) saline + 30mg/kg BW WAY-267,464 (OT agonist); vs. 3) 10mg/kg BW L-368,899 (OTr antagonist) + WAY-267,464, vs. 4) 10 mg/kg BW L-368,899 + saline.	Highly novel environment (brightly lit arena): access to sweetened condensed milk (diluted in water 1:3), latency to begin consumption (sec) measured; no access to food or water during testing.	WAY-267,464 effect (i.e. ↓ anxiety hyponeophagia) abolished by pre-treatment with L-368,899, at 10 mg/kg b. wt. No effect for all other test conditions.	↓
Olszewski et al. (2014)[39] *NZ* Experiment 6	Food intake in familiar environment	Mice BALB/c	6/7 group	M	NR	1 h	12h light/ 12h dark (lights on 0600)	IP OT agonist (WAY-267,464) 3, 10 or 30mg/kg BW vs. saline; injected 5 min prior to feeding (11:00-11:30).	Following overnight fast, familiar environment: ad lib access to chow, food intake measured (g/g BW).	OTr agonist had no effect on familiar chow intake in familiar settings ($p>0.05$).	↔

*Effect of oxytocin agonist administration determined by alteration in dietary intake/behaviours [reported as increase (↑), decrease (↓) or neutral (↔)]. Abbreviations: OT, oxytocin; ICV, intracerebroventricular; LV, lateral ventricle; aCSF, artificial cerebrospinal fluid; OTr, oxytocin receptor; NR, not reported; IP, intraperitoneal; BW, body weight.

Table 4. Description and outcomes of oxytocin gene deletion studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours, days or weeks)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Camerino (2009)[22] *Italy*	Food intake	Mice Hybrid SV129 & C57BL/6J	5 OT KO 5 WT	M & F	2-6 mo	3 x 4 d	NR	OT gene deletion mice vs control	Food intake (standard chow) measured (grams) at 2, 4 and 6 mo. of age.	No significant difference in food intake between OT and WT (hyperphagia-related obesity absent).	↔
Rinaman et al. (2005)[77] *USA*	Food intake and hydration status (euhydrated) vs. dehydrated)	Mice C57BL/6N	7 OT KO 6 WT	M	8-10 mo	1 wk	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	18 h overnight fast: deprived of food alone (fasted, euhydrated) vs. deprived of both food and water (fasted, dehydrated) before 60-min refeeding period (ad lib access to standard chow, +/- water). Food intake measured (grams).	Significant main effect of hydrational state on fasting-induced food intake in WT [F(1,11) 14.77;p<0.003]. Fasted & dehydrated WT consumed significantly less chow during refeeding compared to fasted & euhydrated WT. No significant main effect of hydrational state on food intake in OT KO [F(1,11) 2.17, p= 0.171]. Anorexic effect of water deprivation significantly reduced in OT KO compared with WT.	↔ OT KO ↓in dehydrated WT
Takayanagi et al. (2008)[23] *Japan*	Food intake	Mice hybrid 129/Ola x C57BL/6J	4-8/group	M	8wk	5 wk	NR	OT receptor-deficient mice (OT-/-) vs control (OT+/+)	Ad lib access to standard chow diet or high fat diet, and water. Daily food intake (g/day) recorded.	Daily food intake or circadian rhythm of intake not significantly different between OT+/+ and OT-/- (p>0.05).	↔
Amico et al. (2005)[17] *USA* Experiment 1	Sucrose intake	Mice C57BL/6, F8 generation	8 OT KO 8 WT	F	11-13 mo	4 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Two-bottle choice: 10% sucrose solution vs tap water, available ad lib; intake measured (mL/day). Standard chow available ad lib, intake not recorded.	Cumulative sucrose intake significantly greater in OT KO vs. WT: F(1,14)=25.65, p=0.001; post hoc test, p<0.05 on each day.	↑ in OT KO
Amico et al. (2005)[17] *USA* Experiment 2	Sucrose intake	Mice C57BL/6, F8 generation	8 OT KO 8 WT	F	11-13 mo	4 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Two dish choice: sucrose enriched (30% sucrose by weight) vs standard powdered chow, ~5g	On each day OT KO and WT ate more sucrose diet than standard diet. Days 3 and 4: sucrose-enriched	↑

									fresh food provided daily and water available ad lib; food intake measured (g/day).	chow represented >75% of total food intake for both genotypes, overall F(1,13)=17.9, p<0.001; p<0.05 days 3 and 4 for each genotype.	
Amico et al. (2005)[17] *USA* Experiment 3	Sucrose intake	Mice C57BL/6, F8 generation	8 OT KO 8 WT "sucrose experienced"	F	11-13 mo	4 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Food (grams), sucrose solution (mL), water (mL) and caloric intake recorded during re-exposure to 10% sucrose solution. Standard chow, sucrose solution and water available ad lib.	Day 1 intake of familiar sucrose solution greater than day 1 intake of novel sucrose solution (experiment 1) by same OT KO and WT mice. Overall sucrose solution intake in OT KO vs. WT: F(1,14)=5.45, p=0.035. Overall food intake in OT KO vs. WT: F(1,14)=5.94, p=0.029. No significant difference in overall calorie intake in OT KO vs. WT (p>0.05). Sustained preference for sucrose solution significantly enhanced in female OT KO.	↑ in OT KO
Amico et al. (2005)[17] *USA* Experiment 4	Sucrose intake	Mice C57BL/6, F9 generation	8 OT KO 8 WT	M	5-7 mo	4 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Two-bottle choice: 10% sucrose solution vs tap water, available ad libitum; intake measured (mL/day). Standard chow available ad lib, intake not recorded.	On each day, OT KO consumed significantly greater volumes of sucrose compared with WT cohorts [F(1,14) =14.09, p=0.002; post hoc p< 0.05 on each day	↑ in OT KO
Amico et al. (2005)[17] *USA* Experiment 5	Sucrose intake	Mice C57BL/6, F9 generation	16 OT KO 16 WT	M & F	M=5-7 mo F=age matched	3 x 4 d tests	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Two-bottle choice tests: sucrose solution (test 1=10%, test 2=5%, and test 3=2.5%) vs water. Intakes of water and sucrose solution recorded daily (mL). Standard chow available ad lib, intake not recorded.	At each sucrose concentration, OT KO of both sexes consumed significantly more (approx. double) sucrose solution than WT on day 4 of each test [males: F(1,14)=14.753, p=0.002; females: F(1,14)=30.145, p=0.001]. No significant effect of genotype on preference for different sucrose concentrations.	↑ in OT KO

Amico et al. (2005)[17] *USA* Experiment 6	Sucrose intake	Mice C57BL/6, F8 generation	8 OT KO 8 WT "sucrose experienced"	F	11-3mo	8 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	Two-bottle choice: 10% sucrose solution vs tap water, available ad libitum; intake measured (mL). Standard chow available ad lib, intake not recorded.	OT KO and WT consumed significantly more sucrose solution toward the end of 8-day exposure period relative to beginning [F(7,14)=13.80, p<0.01]. On each day, OT KO drank significantly more sucrose (approx. double) compared with WT [F(1,14)=11.03, p=0.005]. Sustained preference for sucrose solution significantly enhanced in female OT KO.	↑ in OT KO
Miedlar et al. (2007)[78] *USA* Experiment 1	Sucrose intake	Mice C57BL/6, F10 generation	8 OT KO 8 WT	M	5-6 mo	3 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two bottle test: 10% sucrose solution and water ad lib. Intakes recorded daily, day 3 hourly intakes (mL) recorded from 1700 to 2300. Standard chow available ad lib, intake not recorded.	OT KO consumed significantly more sucrose compared to WT mice at each time point [F(1,14)=8.35, p=0.012; t-test, p=0.05].	↑
Sclafani et al. (2007)[18] *USA* Experiment 1	Sucrose intake	Mice C57BL/6	7 OT KO 7 WT	M	14 wk	4 d	12h light/ 12h dark	OT gene deletion mice vs control	Two bottle choice: 10% sucrose solution vs. water, left-right position alternated daily; mean intake (g/day) recorded. Standard chow available ad lib, intake not recorded.	OT KO consumed significantly more sucrose overall than WT [F(1,12)=30.462, p<0.001]. Both groups increased sucrose intake from first 2-day block to second 2-day block [F(1,12)=19.744, p<0.001], OT KO vs. WT significantly greater sucrose preference [block 1: 99% vs. 92%, block 2: 99% vs. 95% in block 2; overall F(1,12)=5.53, p<0.01].	↑
Sclafani et al. (2007)[18] *USA* Experiment 2	Sucrose intake	Mice C57BL/7	7 OT KO 7 WT	M	14 wk	12 d	12h light/ 12h dark	OT gene deletion mice vs control	10% sucrose (operant lick tube) vs. water (bottle). Days 1-4: sucrose available as fixed ratio (FR) schedule; days 5-12: 3 x progressive ratio (PR) schedules (increasing lick	Overall, OT KO consumed more sucrose than WT [F(1,11)=7.816, p<0.05]. Sucrose intake in both genotypes decreased as tests became more demanding [FR schedule:	↑

									requirements to obtain a sucrose reinforcement with each new schedule); mean intake (g/day) recorded. Ad lib access to chow and water.	F(3,33)=63.929, p<0.001] [PR schedule: F(3,33)=64.872, p<0.001]. OT KO obtained more sucrose reinforcements than WT only during FR test [Group x Test, F(3,33)=4.297, p<0.05]. OT KO vs. WT emitted more total licks for sucrose with considerable variability in this measure (group difference NS).	
Billings et al. (2006)[19] *USA* Experiment 1	Saccharin intake	Mice C57BL/6, F9 generation	7 OT KO 8 WT "sucrose experienced"	F	5-8 mo	4 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two-bottle choice: 0.2% saccharin solution vs tap water, available ad libitum; intake measured. Daily intake recorded (mL). Standard chow available ad lib, intake not recorded.	Saccharin intake: OT = ≥98%/day, and WT across 4 d = 74-89% of total daily fluid intake. OT KO mice consumed significantly greater volumes of saccharin solution compared to WT [F(1,13)=11.55, p=0.005; post hoc p<0.05]. OT KO significantly greater total daily fluid intake (approx. double) compared to WT [F(1,13)=10.86, p=0.006; post hoc p < 0.05].	↑
Billings et al. (2006)[19] *USA* Experiment 2	Saccharin intake	Mice C57BL/6, F9 generation	7 OT KO 8 WT "sucrose and saccharin experienced"	F	5-8 mo	4 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Re-exposure to saccharin. Two-bottle choice: 0.2% saccharin solution vs tap water, available ad libitum. Daily intake recorded (mL). Standard chow available ad lib, intake not recorded.	OT KO same preference for saccharin when re-exposed = ≥97%/day. Daily ingestion of saccharin solution significantly greater in OT KO than WT by 1.5- to two-fold, [F(1,13)=5.60, p=0.03]. Daily water intake in both groups minimal (<5% of total fluid intake).	↑
Miedlar et al. (2007)[78] *USA* Experiment 2	Lipid intake	Mice C57BL/6, F10 generation	8 OT KO 8 WT	M	5-6 mo	3 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two bottle test: 10% Intralipid emulsion and water ad lib. Intakes recorded daily (mL), day 3 hourly intakes recorded from 1700 to 2300. Standard chow available	OT KO: immediate and sustained preference for Intralipid emulsion on 1st day of exposure (98% intake), WT: incremental increase in preference	↑ day 1 only

									ad lib, intake not recorded.	(56% on day 1, 70% on day 2, and 86% on day 3). Significant interaction between genotype and exposure day on Intralipid intake across the 3 days of exposure [F(2,28) =4.568, p=0.019]	
Miedlar et al. (2007)[78] *USA* Experiment 3	Lipid intake	Mice C57BL/6, F10 generation	8 OT KO 8 WT (lipid experienced)	M	5-6 mo	3 x 3 d (48 h intervals between tests)	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	3 x two-bottle tests: 1) 10% Intralipid emulsion and water; 2) 5% Intralipid emulsion and water; 3) 2.5% Intralipid emulsion and water. Intakes recorded daily (mL), day 3 hourly intakes recorded from 1700 to 2300. Standard chow available ad lib, intake not recorded.	No significant differences between genotypes in intake of 10%, 5% or 2.5% Intralipid emulsion over 3 days of exposure (80-90% intake on all 3 days for both groups).	↔
Miedlar et al. (2007)[78] *USA* Experiment 4	Lipid intake	Mice C57BL/6, F11 generation	8 OT KO 8 WT	F	5 mo	3 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two bottle test: 4.1% Intralipid emulsion (isocalorically matched to 10% sucrose) and water ad lib. Intakes recorded daily (mL), day 3 hourly intakes recorded from 1700 to 2300. Standard chow available ad lib, intake not recorded.	OT KO: preference for Intralipid, 96% on day 1, 97% on day 2, and 87% on day 3. WT: preference for Intralipid, 58% on day 1, 97% on day 2, and 98% on day 3. Significant difference between OT KO and WT intakes on day 1 only [F(2,28) =4.622, p=0.018]. Effect similar to exposure in naive male OT KO mice (exp. 1b).	↑ day 1 only
Miedlar et al. (2007)[78] *USA* Experiment 5	Lipid intake	Mice C57BL/6, F10 generation	8 OT KO 8 WT	F	13–16 mo	4 x 3 d (48 h intervals between tests)	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	4 x two-bottle tests: 1) 1.0% Intralipid emulsion and water; 2) 2.1% Intralipid emulsion and water; 3) 4.1% Intralipid emulsion and water; 4) 8.2% Intralipid emulsion and water. Chow available ad lib. Food (grams) and fluid (mL) intake recorded daily; data from 3rd day of exposure compared.	Significant effect of concentration on volume consumed [F(1,4)=8.25, p=0.001], but no intake differences between OT KO and WT. Intralipid consumption increased as concentration increased up to 4.1%, declined during 8.2% exposure. Total daily caloric intake (powdered chow + Intralipid) did not differ among Intralipid	↔

										concentrations or between genotypes. No difference between genotypes in calories obtained from powdered chow, but significant effect of Intralipid concentration [F(1,4)=15.99, p<0.001].	
Vollmer et al. (2013)[81] *USA* Experiment 1	Palatable (high NaCl and fat) solution intake	Mice (strain not specified)	8 OT KO 8 WT	M	Adult	4 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two-bottle choice test: water vs. palatable 4.1% Intralipid emulsion with 0.5M NaCl (0.45 kcal/mL). Intake (mL) measured daily. Ad lib access to standard chow.	No differences in intake between OT KO and WT mice. Large intakes of palatable solution on all 4 days by both OT KO and WT.	↔
Sclafani et al. (2007)[18] *USA* Experiment 3	Nutrient preference	Mice C57BL/8	7 OT KO 7 WT	M	14 wk	2 d/test	12h light/ 12h dark	OT gene deletion mice vs control	Series of two bottle choice tests: 1) 10% sucrose vs. water; 2) 10% polycose vs. water; 3) 10% cornstarch vs. water; 4) 4% Intralipid vs. water; intakes measured (grams). Standard chow access NR.	Overall, OT KO consumed more nutrient than WT [F(1,12)=19.820, p<0.001]. Intakes of nutrient type varied [F(3,36)=31.277, p<0.001], and significant Group x Nutrient interaction [F(3,36)=5.508, p<0.01]. Post hoc tests: significant effects of genotype on sucrose, Polycose, and cornstarch intake (p<0.05 for each nutrient); Intralipid intake in OT KO and WT not significantly different (p=0.062). Within-group analyses: OT KO consumed more Intralipid than each of the CHO solutions (p<0.05 for each comparison) and consumed more sucrose and Polycose than cornstarch [F(3,18)=34.377, p<0.001]. WT consumed more Intralipid than each of the CHO solutions (p<0.05 for each	↑sweet and non-sweet CHO ↔ lipid

										comparison), WT consumed similar amounts of sucrose, Polycose, and cornstarch [F(3,18)=14.449, p<0.001]. Groups did not differ in their preferences for sucrose, cornstarch, or Intralipid (98–99%); OT KO had stronger preference (p<0.05) for Polycose than WT [99% vs. 92%; Group x Nutrient, F(3,36)=3.084, p<0.05].	
Amico et al. (2001)[20] *USA*	Sodium intake	Mice C57BL/6, F3 generation	6 OT KO 7 WT	M	9-13 mo	4 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two-bottle choice: 0.5 M (2.9%) NaCl solution vs. tap water. Food available ad lib. At 1600 on day 3, bottles and chow removed; fluids reintroduced at 1000 on day 4. Volume ingested (mL) recorded in 1st hr; chow reintroduced at 1100 and fluid intake (mL) recorded for ensuing 6 hr, food intake not recorded.	After fluid deprivation OT KO ingested greater amount of saline, but not water, in 1st hour (p<0.001) compared with WT. Differences persisted over ensuing 5 h, (p= 0.02). Amount of NaCl solution consumed in both OT KO and WT less than when mice allowed access to food during the fluid deprivation (as in experiment 1). When only water was reintroduced after fluid deprivation, water intake was not different between groups at 1 h (p>0.05) or 6 h (p>0.05).	↑ in OT KO
Amico et al. (2003)[79] *USA* Experiment 1	Sodium intake	Mice C57BL/6, F4 generation	8 OT KO intact, 9 WT intact, 5 OT KO ovariectomised, 6 WT ovariectomised	F	12-14 mo	5 d	12h light/ 12h dark (lights at 0700)	OT gene deletion mice vs control	Two-bottle choice: 0.5 M (2.9%) NaCl solution vs. tap water; volume ingested (mL) recorded daily. At 1600 on day 4, bottles removed and both reintroduced at 1000 on day 5. Volume ingested recorded in 1st hr and for ensuing 6 hr. Food available ad lib, food intake not recorded. Mice restudied following	3 d NaCl solution ingestion not significantly different between genotypes: intact mice [F(1, 15)=1.12, p=0.30], ovariectomized mice [F(1,9)=2.82, p=0.10]. No significant difference between intact OT KO and intact WT in 1st hr after reintroduction of fluid (p=0.27); by 6 hr intact OT KO ingested twofold	↑ in OT KO intact

									ovarectomy, same protocol.	greater amount of NaCl solution than intact WT (p=0.03). Ovariectomised OT KO and WT consumed significantly less NaCl solution after overnight fluid deprivation than intact mice (intact OT KO vs. ovariectomised OT KO at 1 hr, p=0.03, at 6 hr, p=0.02; intact WT vs. ovariectomised WT at 1 hr, p=0.43, at 6 hr, p=0.01). No difference in volume NaCl ingestion at 1 hr (p=0.73) and 6 hr (p=0.44) in ovariectomised genotypes. No difference between groups for water intake.	
Amico et al. (2003)[79] *USA* Experiment 2a & b	Sodium intake	Mice C57BL/6, F4 generation; intact and ovariectomised	a) 7/group intact OT KO and WT, 7/group ovariectomised OT KO and WT b) 7/group ovariectomised OT KO and WT	F	12-14 mo	a) 3 d b) 7 d	12h light/ 12h dark (lights on at 0700)	OT gene deletion mice vs control	a) 3 day two-bottle choice: 0.2 M (1.2%) NaCl solution vs. tap water; volume ingested (mL) recorded daily. b) 7 d two-bottle choice: 0.2 M (1.2%) NaCl solution vs. tap water; volume ingested recorded daily. At 1600 on day 6, bottles removed and both reintroduced at 1000 on day 7. Volume ingested (mL) recorded in 1st hr and for ensuing 6 hr. Standard chow available ad lib, intake not recorded.	a) No significant difference between intact [F(1,12)=0.31, p=0.58] or ovariectomised F(1, 12)=2.52, p=0.12] OT KO and WT for overall 3 d intake. b) Ovariectomised OT KO consumed significantly greater amounts of NaCl solution than matched WT during 6 d test [F(1,12)=19.82, p<0.0001]. Increased salt consumption accompanied by lower water intake in OT KO than WT [F(1, 12)=14.86, p=0.0002]. After overnight fluid deprivation ovariectomised OT KO mice ingested threefold greater amount of NaCl solution than ovariectomised WT in 1st hr after reintroduction of	a) ↔ b) ↑ in OT KO

										fluids (p=0.03), and twofold greater at end of 6 hr (p=0.12). Water intake was lower in OT KO than WT at 1 hr (p=0.03) and at 6 hr (p=0.04) after reintroduction of fluids.	
Puryear et al. (2001)[21] *USA*	Sodium intake	Mice C57BL/6N, F3 generation	7 OT KO 6 WT	M	NR	6 d	12h light/ 12h dark (lights on 0500)	OT gene deletion mice vs control	Two bottle choice: 2% NaCl solution vs. water; salt licking activity (licks/24 h) and volume consumed (mL/24 h) measured.	Six-fold increase in salt licking in OT KO vs. controls (p<0.05); group effects [F7.28, p<0.02] and intake effects [F12.71, p<0.004]. Increased salt intake (volume solution consumed) in OT KO vs. controls (p<0.01); intake effects [F63.0, p<0.001] and interaction effects [F4.57, p<0.05].	↑
Vollmer et al. (2006)[80] *USA* Experiment 2	Sodium intake	Mice C57BL/6 F4 & F5 generations	8 OT KO 8 WT	M	NR	3 d/test	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two-bottle choice tests: NaCl solution (test 1=0.2M, test 2=0.3M, and test 3=0.5M) vs water. Intakes of water and NaCl solution (mL) recorded daily, day 3 intake used for analysis. Standard chow available ad lib, intake not recorded.	Volume of saline consumed decreased as concentration of NaCl increased [F(1,42)=10.97, p<0.001). Volume of 0.2 M NaCl consumed was greater than either 0.3 M NaCl or 0.5 M NaCl (p<0.05). No significant differences between OT KO and WT for any of the volumes ingested.	↔
Vollmer et al. (2006)[80] *USA* Experiment 3	Sodium intake	Mice C57BL/6 F4 & F5 generations	6/group OT KO 6/group WT	M	NR	1 wk	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Days 1-14: mice maintained on either low sodium (0.01% NaCl), regular sodium (1.0% NaCl) or high sodium (8.0% NaCl) test diet (2 groups/diet = OT KO vs. WT). Intake (grams) measured. Ad lib access to test diet and water. Days 8-14: two bottle choice test, 0.5M NaCl solution vs. water, intake measured daily (mL). Ad lib access to test diet.	Days 1-7: OT KO and WT consumed equivalent amounts of test diets. No difference in food or water intake between genotypes. Days 8-14: water and NaCl solution consumptions not significantly different between OT KO and WT.	↔

Vollmer et al. (2006)[80] *USA* Experiment 4	Sodium intake	Mice C57BL/6 F4 & F5 generations	6 OT KO 6 WT	M	NR	10 d	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Days 1-3: only water provided (control period); Days 4-7: only 0.5M NaCl solution available; Days 8-10: only water provided. Standard chow available ad lib days 1-10. Fluid (mL) and food (grams) intake measured daily.	Fluid and food intakes not different between OT KO and WT. Days 1–3: OT KO and WT consumed equivalent amounts of food and water. Days 4-7: gradual significant increase in total daily volume of fluid ingested [$F(6,60)=6.8$, $P=0.001$]. Food intake decreased significantly when only 0.5 M NaCl provided. Day 8-10: greater intake than control period or NaCl only period.	↔
Vollmer et al. (2013)[81] *USA* Experiment 5	Sodium intake	Mice (strain not specified)	7 OT KO 7 WT	M	Adult	2 wk	12h light/ 12h dark (lights on 0700)	OT gene deletion mice vs control	Two-diet choice test: week 1, low (0.01% NaCl) vs regular (1.0% NaCl) sodium diet; week 2, low (0.01% NaCl) vs. high (8.0% NaCl) sodium diet. Intake measured daily (grams). Ad lib access to water.	No differences between OT KO and WT. OT KO and WT consumed significantly more regular sodium diet than low sodium diet in the first week $F(1,12)=21.3$, $p<0.001$. In second week, OT KO and WT consumed equivalent amounts of low and high sodium diets.	↔

*Effect of oxytocin gene deletion determined by alteration in dietary intake/behaviours [reported as increase (↑), decrease (↓) or neutral (↔)]. Abbreviations: OT, oxytocin; OT KO, oxytocin knock out; NR, not reported; WT, wild type; NR, not reported; NaCl, sodium chloride.

Table 5. Description and outcomes of oxytocin gene expression studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Duncko et al. (2003)[82] *Slovakia*	Sucrose intake	Rat Sprague-Dawley	7 anhedonic 9 hedonic	M	NR	3 h	12h light/ 12h dark (lights on 0600)	OT gene expression in hypothalamus (PVN)	4 x two bottle preference test (1% sucrose solution and tap water) to separate rats into anhedonic (non-preferring) vs. hedonic (preferring = >60% sucrose solution ingestion).	No difference in OT gene expression between hedonic and ahedonic rats ($p>0.05$)	↔
Hume et al. (2017)[88] *UK*	High sugar intake	Rats Sprague-Dawley	8 treatment (sweetened condensed milk access) 6 control	M	8-10 wk	8 days	12h light/ 12h dark cycle (lights on 0700)	Activity of OT cells in the hypothalamus PVN and SON: 60 minutes after feeding termination (day 8) rat brains immunostained for c-Fos (marker of neuronal activity).	Schedule-fed sweetened condensed milk (5mL, diluted 50% v/v in water: 40.8kJ, 0.24g fat, 1.68g sugar) 15min access daily during early light phase vs control (no access to SCM); both groups ad lib access to chow and water.	Percentage of SON oxytocin neurons expressing c-Fos significantly increased with voluntary SCM consumption compared with controls (control, 9±1%[a]; SCM, 28±2%[a]; $p=0.0012$). No significant difference in c-Fos expression in PVN OT neurons between the control and SCM groups (control, 5±1%[a]; SCM, 8±2%[a]; $p=0.18$).	↑ (SON) ↔(PVN)
Klockars et al. (2017b)[75] *NZ & USA* Experiment 11	Saccharin intake	Rats Sprague-Dawley	8/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	OTr expression in VMH	Overnight access to 0.1% saccharin solution vs. control (access to water); chow available ad lib.	OTr mRNA expression in VMH unaffected by palatable saccharin consumption ($p>0.05$).	↔
Herisson et al. (2014)[35] *NZ* Experiment 3	CHO vs. non-CHO (saccharin) intake	Mice C57BL/6J	7-8/group "sucrose and saccharin experienced"	M	NR	2 d	12h light/ 12h dark (lights on 0700)	OT gene expression	Consumption of 10% sucrose, 10% corn starch or 0.1% saccharin vs. control (water) following 2 h water deprivation. CHO and saccharin solutions supplied instead of water during 1st 5 hours of dark phase. [Night time chow and	OT gene expression higher in sucrose ($p=0.008$) and corn starch ($p=0.036$) fed groups vs. control. Saccharin did not affect OT mRNA levels.	↑ (sucrose & corn starch); ↔ (saccharin)

									water intakes outside testing hours similar for all groups].		
Herisson et al. (2016)[11] *NZ* Experiment 8	Regular diet vs. sweet + regular diet vs. food deprivation	Rats Sprague-Dawley	8/group	M	Adult	1) 24 h 2) 48 h	12h light/ 12h dark (lights on 0700)	OT gene expression	1) Ad lib access to chow and water (control) vs. 24 h food deprivation. 2) Chow and water (control) vs. chow and 0.1% saccharin solution (instead of water).	Expression of OT mRNA in nucleus accumbens core significantly higher in food-deprived compared to ad lib fed rats (p=0.033). Expression decreased in rats given 48h access to saccharin solution compared to standard diet-fed rats (p=0.045).	↑ in food deprived, ↓ in saccharin fed
Mitra et al. (2010)[83] *USA*	High-sucrose (HS) vs. bland corn starch (CS) diet	Rats Sprague-Dawley	14 HS diet 14 CS diet	M	NR	21 d	12h light/ 12h dark (lights on 0700)	Activity of OT cells in hypothalamus: 60 min after feeding termination (day 21) rat brains immunostained for OT and c-Fos (marker of neuronal activity)	HS or CS powdered diet for 20 days (chronic condition). Day 21, half the rats in the HS group and half in CS group given opposite diet (acute condition). Food available for 2 h (1st half of light cycle). Water available ad lib.	No significant differences in sucrose vs. starch intake (grams) from days 1–20 (chronic condition). Day 21: effect of chronic diet [F(1,24)=6.95, p=0.014] and effect of acute diet [F(1,24)=10.22, p=0.004], and interaction approaching significance (p=0.053). Sucrose-starch group (i.e. rats received sucrose day 1–20, and starch day 21) had significantly lower intake on final day vs. sucrose-sucrose [t(12)=5.134, p=0.01], starch-starch [t(12)=3.175, p=0.08] and starch-sucrose [t(12)=4.404, p=0.001] groups. Percentage of c-Fos-positive OT cells in PVN [F(1,24)=9.76, p=0.005] and SON [F(1,24)=6.92, p=0.015] significantly lower in rats chronically exposed to HS vs. CS diet. No effect of acute diet in PVN or SON. Rats receiving acute diet (regardless of type:	↓ chronic diet ↔ acute diet

										sucrose or starch) had significantly increased density of c-Fos positive nuclei in amygdala [F(1,23)=6.189, p=0.021] and nucleus tractus solitarius [F(1,23)=7.551, p=0.011]; increased density of c-Fos-positive nuclei detected in PVN (p = 0.062) and SON (p=0.090). Effect seen acute diet.	
Olszewski et al. (2009)[84] *USA*	Sweet vs. regular diet	Rats Sprague-Dawley	8 treatment 8 control	M	Adult	14 d	12h light/ 12h dark (lights on 0700)	OT gene expression in hypothalamus. Brain tissue excised 2-4 h after end of last meal.	Sweet (Teklad F0078 = 3.75kcal/g, 61.5% CHO, 18.8% protein, 5.0% fat, 4.6% fibre and 4.4% ash) vs. regular (Teklad 8604 = 3.93 kcal/g, macronutrient composition NR) diet, ad lib access.	Significant difference between in OT gene expression between groups ($p<0.05$); sweet diet group had increased OT gene expression compared to regular diet group.	↑
Olszewski et al. (2015)[61] *NZ* Experiment 2	Sucrose intake	Mice C57BL/6N	8 dyads (1 dominant + 1 subordinate) /group	M	~19 wk	48 h	12h light/ 12h dark (lights on 0700)	OT mRNA levels in hypothalamus.	Mice housed in a social environment with 5h/day access (onset of dark cycle) to a pre-determined amount of 10% sucrose for two days, vs. mice in control setting where sucrose not given. Ad lib access to chow.	In social setting, dominant mice consuming palatable sucrose have higher mRNA levels than their subordinate counterparts (p=0.024). No difference in gene expression between groups when diet not enriched with sucrose (p>0.05).	↑ for sugar diet, dominant mice ↔ for sugar diet, subordinate mice ↔ for standard diet, dominant and subordinate mice
Olszewski et al. (2010)[48] *Sweden* Experiment 5	Sucrose vs. fat intake	Mice C57BL/6J	8 sucrose treatment 8 Intralipid treatment 8 control	M	NR	48 h	12h light/ 12h dark (lights on 0700)	OT gene expression in hypothalamus. Brain tissue excised after 48 h between 1100 and 1200 h.	10% sucrose solution vs. 4.1% Intralipid solution vs. control (chow only), all groups ad lib access to chow. Solutions isocaloric (0.4kcal/g), calorie content of chow 3.6 kcal/g.	Significantly higher increase in c-Fos-positive OT neurons in PVN at termination of Intralipid (p=0.016) or sucrose (p=0.011) intake compared with control group. Increase 2-fold higher in mice fed sugar than fat (p=0.037).	↑↑ (sucrose) ↑ (fat)

										Upregulation of OT mRNA levels (p=0.009) in sucrose group compared to Intralipid group. Controls (fed only chow which is high in CHO) had OT mRNA levels similar to sucrose group (p=0.178) and significantly higher than Intralipid group (p=0.043).	
Olszewski et al. (2010)[48] *Sweden* Experiment 6	Sucrose vs. fat intake	Mice C57BL/6J	7 sucrose preferrers 7 fat preferrers 7 neutral (i.e. no preference)	M	NR	42 d	12h light/ 12h dark (lights on 0700)	OT gene expression in hypothalamus. Day 42: brain tissue excised after 21 day washout phase between 1100 and 1200 h.	Following 7 day preference test, mice given ad lib access to 10% sucrose solution, 4.1% Intralipid solution, and chow [solutions isocaloric (0.4kcal/g), chow =3.6 kcal/g] for 21 days. Day 22-42 (washout phase) access to chow only.	Fat preferrers (39.2±3.0% cal from sucrose)[a], sucrose preferrers (57.0±2.2% cal from sucrose)[a], and neutrals (46.9±1.9% kcal from sucrose)[a] did not differ in their baseline OT mRNA levels.	↔
Pirnik et al. (2012)[85] *Slovak Republic*	High fat diet (HFD) vs. standard diet	Mice C57BL/6N (ovariectomised)	2 HFD 2 Standard diet	F	11 wk	16 weeks	12h light/ 12h dark	Fos expression in OT neurons in PVN. Perfusion between 8:00 and 12:00 to minimise diurnal Fos expression.	HFD (13% protein, 60% fat, 27% CHO) vs. standard diet (macronutrient distribution NR), ad lib access.	Prolonged HFD or standard diet produced negligible Fos expression in OT producing neurons (0.3% vs. 0.6%) in PVN.	↔
Greenwood et al. (2015)[86] *UK & Brazil* Experiment 1	Salt loading (SL) and water deprivation (WD)	Rat Sprague-Dawley (UK) & Wistar (Brazil)	7 SL 7 WD 6 control	M	10-12 wk	7 d (SL) 3 d (WD)	UK: 14h dark/ 10 h light (lights on 0700); BR: 12h dark/ 12h light	OT gene expression in hypothalamus (SON)	SL: replacement of drinking water with 2% NaCl (w/v in tap water), WD: complete fluid deprivation, Control: drinking water ad lib. Standard chow available ad lib to all groups. WD food intake decreased (32-75% less) compared with control ($p<0.0001$). SL food intake similar to control until days 5-7, where dropped significantly ($p<0.0001$).	Significant differences in OT gene expression between WD, SL and control ($p<0.0001$). OT expression in SON elevated in SL and WD.	↑
Silva et al. (2002)[87] *Portugal*	Prolonged alcohol exposure	Rats Wistar	16 EtOH-treated 16 Withdrawal 16 Controls	M	2 mo	6-10 mo	12h light/ 12h dark (lights on 0700)	Number of OT-immunoreactive magnocellular neurons and OT mRNA levels in PVN	3 test conditions: 1) Ethanol-treated: 20% v/v EtOH solution (~9.5g/kg BW EtOH) only available liquid source for 6 or 10	EtOH treated: significant reduction in total number OT-immunoreactive neurons [$F(1,16)=35.09$, $p<5x10^{-4}$], not influenced	↓ OT neurons ↔ OT mRNA

									mo. 2) Withdrawal: EtOH only available liquid source for 6 mo, then water only for 4 mo. 3) Control group. All groups ad lib access to food; liquids supplemented with 300mg/100mL of vitamins and 500mg/100mL of minerals.	by length of EtOH exposure [F(1,16)=3.16, p=0.09]. EtOH-treated vs. withdrawal group: no significant variations in total number of OT-immunoreactive neurons. Withdrawal vs. control group: number of neurons significantly smaller in withdrawn rats [F(2,12)=13.09, p<0.001]. OT mRNA not significantly altered by chronic EtOH treatment and withdrawal [F(2,12)=0.07, p=0.936].	
Klockars et al. (2018)[74] *NZ & USA* Experiment 12	Food deprivation and saccharin intake	Rats Sprague-Dawley	6-8/group	M	Adult	2-24 h	12h light/ 12h dark cycle (lights on 0700)	OTr mRNA expression in BLA	3 conditions before decapitation: 1) Chow deprived 24h, ad lib access to water; vs 2) 48h access to chow and 0.1% saccharin instead of water; vs. 3) control (ad lib access to chow and water).	Significant decrease in BLA OTr mRNA levels [F(2, 18)=5.594; p=0.007] in saccharin-consuming rats compared to controls.	↓ (saccharin) ↔ (food deprivation)
Klockars et al. (2018)[74] *NZ & USA* Experiment 13	Food deprivation and saccharin intake	Rats Sprague-Dawley	6-8/group	M	Adult	2-24 h	12h light/ 12h dark cycle (lights on 0700)	OTr mRNA expression in CNA	3 conditions before decapitation: 1) Chow deprived 24 h, ad lib access to water; vs 2) 48h access to chow and 0.1% saccharin instead of water; vs. 3) control (ad lib access to chow and water).	Food deprivation significantly upregulated CNA OTr expression [F(2, 19)=7.614; p=0.0443] compared to controls.	↑ (food deprivation) ↔ (saccharin)
Klockars et al. (2017b)[75] *NZ & USA* Experiment 10	Food deprivation	Rats Sprague-Dawley	8/group	M	9 wk	2 h	12h light/ 12h dark cycle (lights on 0800)	OTr expression in VMH	Chow deprived overnight vs control (food available ad lib); both groups ad lib access to water.	OTr mRNA expression in VMH elevated in energy-deprived animals compared to ad lib-fed controls (p=0.0404).	↑

Suyama et al. (2016)[41] *Japan*	Fasted vs. fed state	Rats Wistar & Oxt-mRFP transgenic	10-11/group	M	6-7 wk	24 h	12h light/ 12h dark (lights off 1930)	Regulation of synaptic transmission on OT neurons in PVN	Ad lib fed state vs. 24 h fasted state	Under fed condition, compared to 24 h fasted condition, increased excitatory synaptic input on PVN OT neurons ($p<0.05$).	↑
Uchoa et al. (2009)[42] *Brazil* Experiment 2	Fasting vs. refeeding	Rats Wistar	5-6/group	M	NR	16-18 h	12h light/ 12h dark (lights on 0600)	OT neuron activation in PVN and SON	16 h fasting vs. 2 h refeeding	Refeeding increased ($p<0.01$) the percentage and number of Fos/OT immunoreactive neurons in PVN ($p<0..01$) and SON ($p< 0.05$).	↑
Uchoa et al. (2009)[42] *Brazil* Experiment 3	Fasting vs. refeeding	Rats Wistar	5-8/group	M	NR	16-18 h	12h light/ 12h dark (lights on 0600)	OT mRNA expression in PVN and SON	16 h fasting vs. 2 h refeeding	Refeeding did not alter OT mRNA expression in PVN or SON ($p>0.05$)	↔

*Effect of dietary intake/behaviours determined by alteration in oxytocin gene expression [reported as increase (↑), decrease (↓) or neutral (↔)]. [a]Values reported as mean ± S.E.M. Abbreviations: OT, oxytocin; NR, not reported; PVN, paraventricular nucleus; SON, supraoptic nucleus; OTr, oxytocin receptor; VHM, ventromedial hypothalamic nucleus; CHO, carbohydrate; kcal, kilocalorie; NaCl, sodium chloride; EtOH, alcohol; BLA, basolateral nuclei of the amygdala; CNA, central nuclei of the amygdala.

Table 6. Description and outcomes of endogenous oxytocin studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Morton et al. (2012)[38] *USA* Experiment 5	High fat diet (HFD) vs. Low fat diet (LFD)	Rats Sprague-Dawley	7-8 HFD 10 LFD (control)	M	Adult	4 mo	12h light/ 12h dark	Serum OT (following 6 h fast) by ELISA	HFD (45% kcal fat) vs. LFD (10% kcal fat), ad lib access	LFD = ~6ng/mL, HFD = ~4ng/mL, p>0.05 (interpreted from graph)	↔
Zhang et al. (2011)[45] *USA* Experiment 5	High fat diet (HFD) vs. standard diet	Mice C57BL/6	8–10/group	M	Adult	12 wk	12h light/ 12h dark	Diurnal rhythmicity: 24 h profile of diurnal serum OT levels measured by EIA following 12 week intervention	HFD vs. standard chow feeding	Chow fed mice: rapid daytime rise and gradual nighttime decline in OT. HFD fed mice: no diurnal rhythmic change in OT. Chronic HFD abolished OT rhythmicity by suppressing daytime rise.	↓ diurnal rhythmicity
Zhang et al. (2011)[45] *USA* Experiment 6	High fat diet (HFD) vs. standard diet	Mice C57BL/6	6–7/group	M	Adult	12 wk	12h light/ 12h dark	Diurnal rhythmicity: ex vivo OT release from PVN under basal and depolarization (KCl stimulated OT release) conditions following 12 week intervention; at midday vs. midnight.	HFD vs. standard chow diet	Standard diet: depolarization-induced OT release active during daytime, absent during nighttime (diurnal OT release correlated with a feeding circadian pattern). HFD diet: depolarization unable to stimulate daytime or nighttime OT release (feeding circadian arrhythmicity).	↓ diurnal rhythm
Morris et al. (1995)[89] *USA* Experiment 1	Sodium vs. water intake	Rats Sprague-Dawley	Baroreceptor-denervated: 7 treatment (NaCl) 6 control (water) Sham operated (SO): 5 treatment (NaCl) 4 control (water)	M	NR	18 h	12h dark/ 12h light	Plasma OT (via RIA) and posterior pituitary OT content measured	Intake of 2% NaCl solution vs. water measured 18 h period.	Baroreceptor-denervated rats consumed less NaCl than SO group. Plasma OT significantly higher in baroreceptor-denervated rats receiving salt vs water. Salt intake produced no change in plasma OT in the SO group. No significant difference in posterior pituitary OT content between groups.	↑ plasma OT ↔ pituitary OT

Greenwood et al. (2015)[86] *UK & Brazil* Experiment 2	Salt loading and water deprivation	Rat Sprague-Dawley (UK) & Wistar (Brazil)	7 Salt loading (SL) 7 water deprivation (WD) 6 control	M	10-12 wk	7 d (SL) 3 d (WD)	UK: 14h dark/ 10 h light (lights on 0700); BR: 12h dark/ 12h light	Plasma OT via RIA	SL: replacement of drinking water with 2% NaCl (w/v in tap water), WD: complete fluid deprivation, Control: drinking water ad lib. Standard chow available ad lib to all groups. WD food intake decreased (32-75% less) compared with control ($p<0.0001$). SL food intake similar to control until days 5-7, where dropped significantly ($p<0.0001$).	Compared with controls plasma OT higher in SL ($p<0.05$) and WD ($p<0.005$). OT plasma levels significantly lower in SL compared with WD ($p<0.05$).	↑
Hartley et al. (2003)[60] *UK*	Low vs. high soya isoflavone diet	Rats Lister	16 iso-free 16 iso-150	M	8 wk	14 d	12h light/ 12h dark (lights on 0700)	Plasma OT	Iso-free diet (minimal level of soy isoflavones) vs. Iso-150 diet [150 mg/g total isoflavones (genistein + daidzein)]. Diets matched for protein, CHO and fat content.	Food intake (g/day/rat): Iso-150 =9.4±0.2[a], Iso-free =8.6±0.3[a] [$F_{9,54}=4.6$, NS]. Plasma OT (pmol/l): Iso-150 = 17.5±3.5, Iso-free =16.6±2.7 [$F_{1,14}<1.0$, NS]. No difference between groups.	↔
Bjorkstrand et al. (1992)[53] *Sweden*	Food deprivation	Rats Sprague-Dawley	10 food deprived 10 control	M&F	Adult	24h	12h light/ 12h dark cycle (lights on 0700)	Plasma OT via RIA	Food deprived for 24 h vs control (freely fed); both groups ad lib access to water.	Mean (±SD) plasma OT (PM): food deprived females = 25±7 vs freely fed females = 40±12; food deprived males = 21±9 vs freely fed males = 25±8. No significant change in plasma OT in response to food deprivation.	↔
Burlet et al. (1992)[43] *USA*	Fasting vs. refeeding	Rat Sprague-Dawley	8-16/group (2 x treatment, 1 x control)	M	NR	42 h	12h light/ 12h dark (lights on 0600)	OT concentration in hypothalamic nuclei and the neurohypophysis	Control (satiated rats with freely available food) vs. 48 h food deprived rats vs. refed rats (42 h food deprived with subsequent 6 h refeeding, food ad lib). Water available ad lib to all groups.	Food deprivation: no change in OT concentration in pPVN, mPVN and SON; significant decline (-36%; $p < 0.05$) in median eminence (ME). Effect not significantly reversed by refeeding. OT in neurohypophysis unaffected by food deprivation and subsequent refeeding ($p>0.05$). Food intake	↓ ME ↔ pPVN, mPVN and SON

							during 6 h refeeding >50% of usual 24 h intake under ad lib-fed state.

*Effect of dietary intake/behaviours determined by alteration in oxytocin gene expression [reported as increase (↑), decrease (↓) or neutral (↔)]. [a]Values reported as mean ± S.E.M. Abbreviations: OT, oxytocin; ELISA, enzyme-linked immunosorbent assay; EIA, enzyme immunoassay; PVN, paraventricular nucleus; KCl, potassium chloride; RIA, radioimmunoassay; NaCl, sodium chloride; pPVN, parvocellular neurons of paraventricular nucleus; mPVN, magnocellular neurons of the paraventricular nucleus; SON, supraoptic nucleus.

Table 7. Description and outcomes of 'other' oxytocin studies

Author (year) *Country*	Dietary characteristic studied	Subjects	n	Sex	Age (weeks or months)	Testing duration (hours or days)	Light/ dark cycle	OT measure	Dietary measure	Relationship between diet and OT	Overall effect* [Increase/ Decrease/ Neutral]
Bahi et al. (2016)[90] *UAE* Experiment 1	Alcohol intake	Mice C57BL/6	12 OTr 12 Mock	M	NR	5 x 5 d	12h light/ 12h dark (lights on 0600)	OTr overexpression vs. mock controls (injected in the nucleus accumbens)	5 x Two-bottle choice tests: ethanol (test 1=2.5%, test 2=5%, test 3=10%, test 4=15% and test 5=20%; v/v) vs water. Intakes of ethanol (g/kg) and water (mL/kg) recorded daily. Standard pelleted chow available ad lib, food intake not recorded. Bottle positions (left/right) were interchanged daily	Between subjects main effect on voluntary ethanol consumption [$F(1,22)=64.207$, $p<0.0001$]. Significant effect of ethanol concentration [$F(4,88)=116.921$, $p<0.0001$]. OTr drank significantly less than Mock at the four higher (5%: $p<0.0001$; 10%: $p=0.002$; 15% and 20%: $p<0.0001$), but not lower (2.5%: $p=0.145$) concentrations. Lower ethanol preference in OTr vs. Mock at higher (5, 10, 15 and 20%: $p<0.0001$) but not at lower (2.5%: $p=0.084$) concentrations. Total fluid intake not different between groups ($p=0.718$).	↓
Bahi et al. (2016)[90] *UAE* Experiment 2	Sweet and bitter taste preference	Mice C57BL/7	12 OTr 12 Mock	M	NR	4 x 5 d	12h light/ 12h dark (lights on 0600)	OTr overexpression vs. mock controls	Two-bottle choice tests: saccharin (test 1=0.035%, test 2=0.07%) vs. water; quinine (test 3=35µM, test 4=70µM) vs water. Saccharin (g/kg), quinine (mg/kg) and water (mL/kg) intake recorded daily. Standard chow available ad lib, intake not recorded. Bottle positions (left/right) were interchanged daily serially.	Increased preference for higher saccharin concentration in both OTr and Mock [$F(1,22)=348.394$, $p<0.0001$]. No differences in sweetener intake between groups [$F(1,22)=0.339$, $p=0.567$]. Total fluid intake (saccharin + water) did not differ between groups [$F(1,22)=0.130$, $p=0.722$]. Less preference for higher quinine concentration in	↔

										both OTr and Mock [F(1,22)=9.371, p=0.006]. No differences in quinine intake between groups [F(1,22)=0.442, p=0.513]. Total fluid intake (quinine + water) did not differ between groups (p=0.975).	
Ryan et al. (2017)[54] *USA* Experiment 1	Food intake	Mice C57BL/6J $Oxtr^{Cre/+}$	7 treatment (injected with hM3Dq) 7 control (injected with mCherry)	M	7-14 wk	2 h	12h light/ 12h dark cycle	Activation of OTr neurons in PBN vs control; 30min prior to testing treatment group injected with CNO (synthetic ligand clozapine-N-oxide).	1) Baseline food intake (standard chow) measured start of dark cycle. 2) Following 24 h fast, food intake (standard chow) measured in the morning.	OTr stimulation in PBN had no significant effect on food intake at baseline or after 24 h fast. Baseline food: interaction F(8,96)=0.2901, p=0.9678; 24 h fast: interaction F(8,96)=1.143, p=0.3424.	↔
Ryan et al. (2017)[54] *USA* Experiment 2	Liquid diet intake	Mice C57BL/6J $Oxtr^{Cre/+}$	6 treatment (injected with hM3Dq) 7 control (injected with mCherry)	M	7-14 wk	2 h	12h light/ 12h dark cycle	Activation of OTr neurons in PBN vs control; 30min prior to testing treatment group injected with CNO (synthetic ligand clozapine-N-oxide).	Following 24 h fast, liquid diet intake (Ensure nutrition drink) measured in the morning; ad lib access to water.	Both groups showed preference for hypercaloric solution, consuming more Ensure than water. No significant difference between groups for Ensure [F(8,88)=0.3808, p=0.9282] or water intakes [F(8,88)=0.5037, p=0.8505].	↔
Ryan et al. (2017)[54] *USA* Experiment 3	Sodium intake	Mice C57BL/6J OxtrCre/+	7 treatment (injected with hM3Dq) 7 control (injected with mCherry)	M	7-14 wk	2 h	12h light/ 12h dark cycle	Activation of OTr neurons in PBN vs control; 30min prior to testing treatment group injected with CNO (synthetic ligand clozapine-N-oxide).	Following 24h dehydration and sodium depleted diet, two-bottle choice test: 0.3M NaCl vs. water, at start of dark cycle. Fluid intake measured at 15min intervals. Ad lib access to food (sodium-depleted diet).	Significant decrease in NaCl and water intake in the presence of food. NaCl: interaction F(8,96)=12.63, p<0.0001; water: interaction F(8,96)=39.75, p<0.0001.	↓
Ryan et al. (2017)[54] *USA* Experiment 4	Sodium intake	Mice C57BL/6J OxtrCre/+	6 treatment (injected with hM3Dq) 6 control (injected with mCherry)	M	7-14 wk	2 h	12h light/ 12h dark cycle	Activation of OTr neurons in PBN vs control; 30min prior to testing treatment group injected with CNO (synthetic ligand clozapine-N-oxide).	Following 24h dehydration and sodium depleted diet, two-bottle choice test: 0.3M NaCl vs. water, at start of dark cycle. Fluid intake	Significant decrease in NaCl and water intake in the absence of food. NaCl: interaction F(8,80)=8.173, p<0.0001; water:	↓

									measured at 15min intervals. No access to food.	interaction F(8,80)=22.31, p<0.0001.	
Ong et al. (2017)[56] *USA* Experiment 1	Food intake and meal pattern	Rats Sprague-Dawley	8 KD 15 control (non-virus injected)	M	NR	24 h	12h light/ 12h dark cycle	Virally mediated OTr knockdown; virus injected into NTS 2wk prior to testing.	Cumulative food intake (grams), meal size (grams) and meal number measured for 24 h and averaged across 2 days. Powdered chow available ad lib.	Overall effect of group [F(1,21)=4.43, p<0.05), time [(F10,120)=28.43, p<0.001] and group x time interaction [(F10,120)=2.47, p<0.01) on meal size. Meal sizes at 3 h, 4 h, 8 h, 12 h, and 24 h after dark cycle onset greater in KD compared with controls (p<0.05). For meal number, significant effects on time (F10,120 = 399.29, P , 0.001) and group x time interaction (F10,120 = 5.12, P ,0.001). KD rats consumed fewer meals at 8 h and 24 h after dark cycle onset when compared with controls (p<0.05). Combination of larger meal size and fewer meals taken resulted in absence of an effect on cumulative chow intake between KD and controls [(F1,21)=1.74, NS].	↑ meal size, ↓ number meals, ↔ overall food intake
Ong et al. (2017)[56] *USA* Experiment 2	Food intake	Rats Sprague-Dawley	8 satiated OTr knockdown (KD) 9 satiated control (non-virus injected)	M	NR	1.5 h	12h light/ 12h dark cycle	Virally mediated OTr knockdown; virus injected into NTS 2wk prior to testing.	Rats given preload (12mL Ensure; 1.42kcal/mL) to induce satiation 10min prior to dark onset and chow presentation. Chow intake measured 0.5 h, 1 h and 1.5 h.	Controls significantly reduced chow intake at 0.5 h, 1 h and 1.5 h (p<0.01). No overall effect of preload volume [F2,14 = 1.76, NS] on chow intake in KD. Significant main effect of time [(F2,14)=29.74, p<0.001]. No difference at 24h in food intake between control and KD	↔

										whether rats were given 0mL (control: 25.4±1.3 g, KD: 27.8±0.9g[a]; NS), 7mL (control: 27.2±1.5 g, KD: 28.5±0.7g[a]; NS), or 12 mL (control: 27.5±1.1g[a], KD: 29.1±0.9g[a]; NS) preload.	
Ong et al. (2017)[56] *USA* Experiment 3	Food intake	Rats Sprague-Dawley	7 OTr knockdown (KD) 9 control (non-virus injected)	M	NR	4 h	12h light/ 12h dark cycle	Virally mediated OTr knockdown; virus injected into NTS 2wk prior to testing.	Following 24h food deprivation, food intake measured at 0.5h, 1 h and 1.5 h after dark onset.	Main effect of group [(F1,14) = 6.54, p<0.05] and time (F2,28)=28.14, p<0.0001) on chow intake following 24 h fast. At 0.5 h and 1 h after refeed, KD consumed significantly more chow than controls (p< 0.05). Chow intake not different between groups at 1.5h 2h (control: 12.6±0.7g[a], KD: 14.3±0.7g[a]; NS), or 3h (control: 14.9±0.4g[a], KD: 15.5±0.9g[a]; NS) time points.	↑(0.5h and 1h)
Wu et al. (2012)[91] *USA*	Food intake	Mice Oxytocin-Ires Cre	6-7 lesion 6-7 control	M	14-15 wks	1 wk	12h light/ 12h dark	OT neuron lesion mice vs. control	Ad lib access to either 1) standard chow, or 2) high fat diet (HFD). Intake measured daily (grams).	No difference in food intake between genotypes on either chow or HFD diet (p>0.05).	↔
Morris et al. (1995)[89] *USA* Experiment 2	Sodium intake	Rats Sprague-Dawley	Baroreceptor-denervated: 5 treatment (OT antisense) 6 control (mixed-base ODNs) Sham operated (SO): 7 treatment (OT antisense) 4 control (mixed-base ODNs)	M	NR	24 h	12h light/ 12h dark	ICV PVN injection of OT antisense [unmodified antisense ODNs (oligodeoxynucleotides)] or control: 2.0µg/0.3µ1 mixed-base ODNs. [ODNs offer specificity which is not available with OTr antagonists). Injection given before feeding.	2% NaCl solution given as sole drinking fluid for 24 h period. Intake measured (mL).	Decrease in salt intake in baroreceptor-denervated treatment group vs. control (p < 0.05). No difference in SO group between treatment and control groups.	↔

*Effect of oxytocin measure determined by alteration in dietary intake/behaviours [reported as increase (↑), decrease (↓) or neutral (↔)]. [a]Values reported as mean ± S.E.M. Abbreviations: OT, oxytocin; NR, not reported; OTr, oxytocin receptor; PBN parabrachial nucleus; KD, knock down; NS, not significant; NTS, nucleus tract solitaries; kcal, kilocalorie; PVN, paraventricular nucleus; NaCl, sodium chloride.

Table 8. Experimental route, site, and dose of exogenous oxytocin administration

Route and site of administration	Number of experiments	Dosage ranges
Infusions		
Peripheral	13[16,33,50,55,58,59]	36-1600µg/kg/day, or 5-50nmol/day
Intracranial (third or fourth ventricle)	12[16,57]	16-200nmol/day
Peripheral Injections		
Intraperitoneal	37[9,10,12-15,36-38,40,45,47,49,50,52,55,69]	~17-10,000µg/kg, or ~22.5-1200mU/kg
Subcutaneous	8[55,62,65-67]	1.0mg/kg, or 0.5mL x 11 to 22µg, or 0.5mL x 5-10IU/mL, or 1,600µg/kg
Intravenous	10[73]	0.03-0.3µg/kg
Intracranial Injections		
Lateral ventricle	15[13-15,40,49,51,63,64,68,70,72]	1.0-10.0µg, or 0.5µg/2L, or 1.0µg/5L, or 0.1-10.0IU, or 0.5-20nmol, or 0.4nmol/0.5µl
Third ventricle	2[38,45]	1.0µl
Nucleus accumbens (core or shell)	5[11]	0.03-3.0µg
Ventromedial hypothalamic nucleus	9[46,75]	0.1-1.0nmol, or 0.3-1.0 µg
Ventral tegmental area	1[71]	0.3-1.0µg
Arcuate nucleus	1[51]	0.4nmol/0.5µl
Basolateral or central nuclei of amygdala	7[74]	0.1-1.0µg
Topical		
Intranasal	1[37]	0.1-10µg/10µl