Effects of single-session versus multi-session non-invasive brain stimulation on craving and consumption in individuals with drug addiction, eating disorders or obesity: A meta-analysis

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and over were defined as obese (Health United States Report 2016; [2]), with a cumulative lifetime risk of eating disorders characterized by excessive eating of 5.7% of the population (National Comorbidity Survey Replication 2001–2003; [3]). Novel treatment

included individuals with alcohol and nicotine addictions [41,44], but not illicit drug users. Fifth, the current meta-analysis addressed potential infl

potential influences of the population, stimulation technique and study design on such intervention effects. In particular, as five studies [56−60] included both left and right dlPFC stimulation data, in order to exclude the multiple effect sizes in individual studies, we used Z-test (instead of Q-test) to assess the potential influences of the stimulated hemisphere [63]. Furthermore, we used Egger's regression intercept test to measure for publication bias [68]. All suitable data were calculated with the software Comprehensive Meta-Analysis 2.0 (CMA) (http://www.meta-analysis 2.0.com).

Results

The results of the initial search are summarized in Fig. 1. We included a total of 48 studies focusing on non-invasive brain stimulation interventions in drug or eating addiction. The characteristics of these studies are summarized in Table 1. Not all studies reported both craving and consumption measures, and only 5 studies evaluated both a single-session and a multi-session effect (Supplementary Table 1). Specifically, we included 44 articles on studies assessing the overall intervention effect of brain stimulation on craving (33 with single-session and 15 with multi-session interventions). In addition, we included 15 articles on studies that investigated the overall intervention effect of brain stimulation on consumption (10 with single-session and 7 with multi-session interventions). All included studies used excitatory rTMS or tDCS stimulation.

Assessment of risk of bias in the included studies

The evaluation of the risk of bias for each included study was summarized in Supplementary Table 2. The results indicated that overall the included studies were of high quality (i.e., at relatively low risk of bias). In addition, the evaluation of the control condition and blinding procedures for all included studies was summarized in Supplementary Table 3. Both evaluations found that all included

Table 1
Study and sample characteristics for included studies.

First author	Study population	Number of sessions (per condition)	Anodal Stimulation side (dlPFC)	Stimulation Technique	Participants number	Study Design	total number of pulses (per condition)	Craving measure	Consumption measure
Alcohol (12 studies)									

Fecteau et al.(2014)	Average daily intake of at least 15 cigarettes	Craving: Both 1 and 5; Consumption: 5 Craving: 5	Self-report Cigarettes consumed *

protocols were more beneficial. However, the moderator analysis testing for a positive linear association between the number of

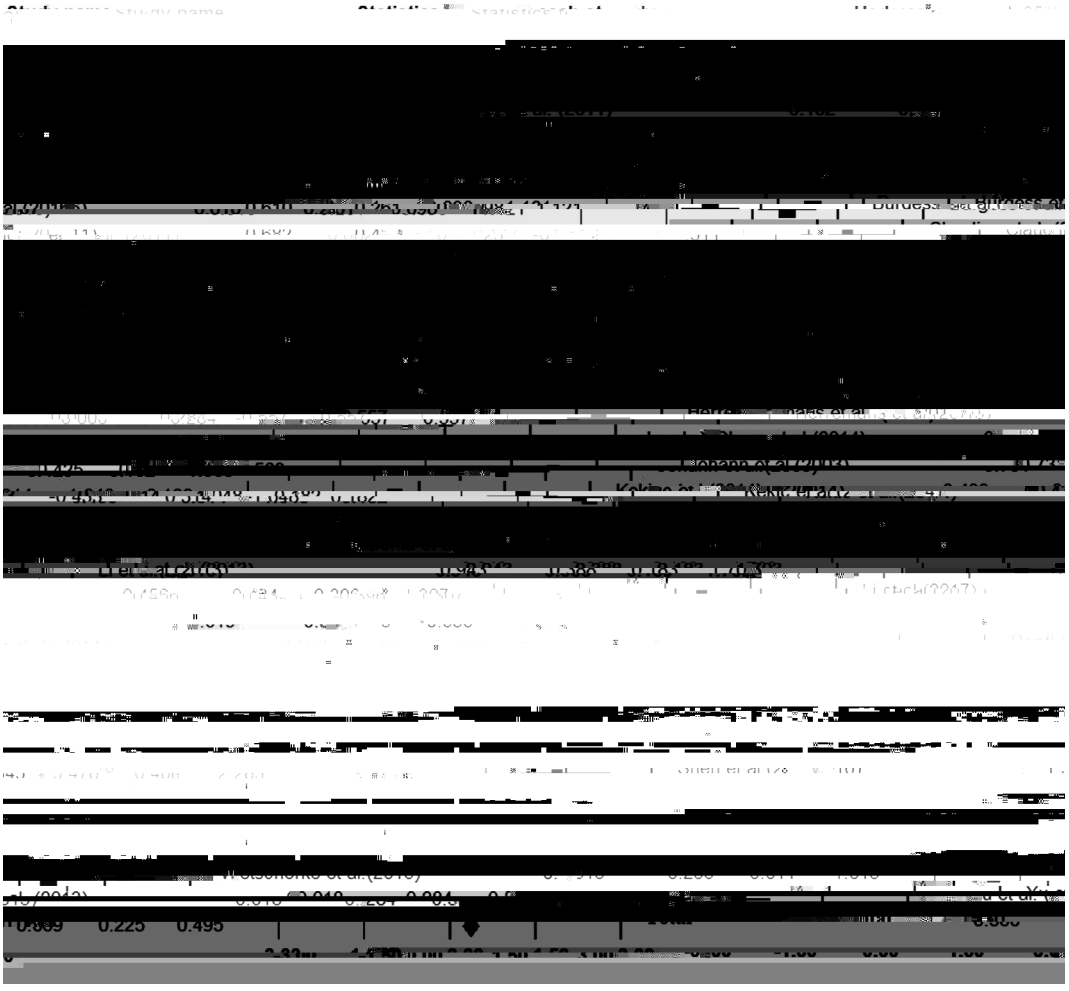

Fig. 3. The effect of single-session neuromodulation on craving.

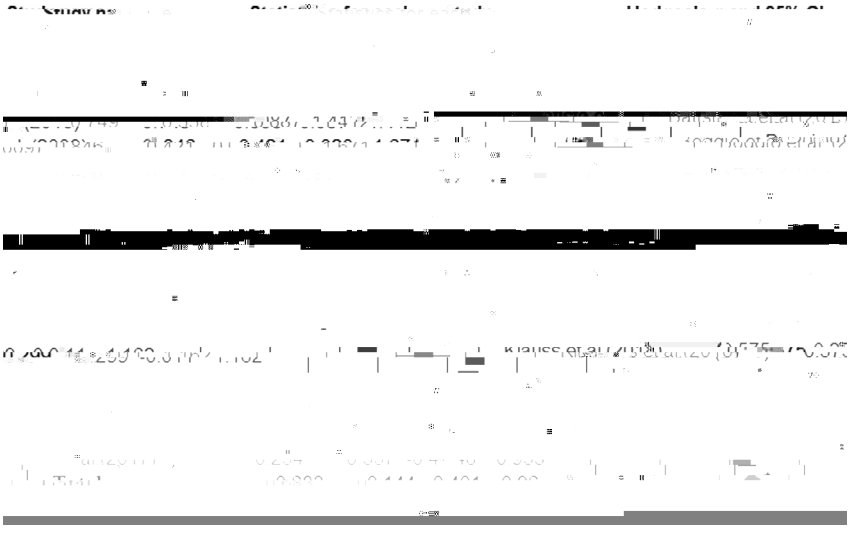

Fig. 4. The effect of multi-session neuromodulation on craving.

$p = 0.085$), revealing a slightly larger effect in individuals with nicotine addiction (with consumption levels generally being measured by cigarettes smoked per day as indicated by self-report, see Table 1) as compared to eating addiction (based on consumed food during a test after the intervention, see Table 1). When considering these two populations separately, we found a significant reduction of consumption levels in both populations, with a large effect size in smokers ($g = 1.138$, CI: 0.543–1.733; $z = 3.751$,

Fig. 5. Regression of the total number of pulses on the effect size of neuromodulation of craving. β = 0.0001, 95% CI: 0.00002–0.00013, Q = 8.465, p = 0.004.

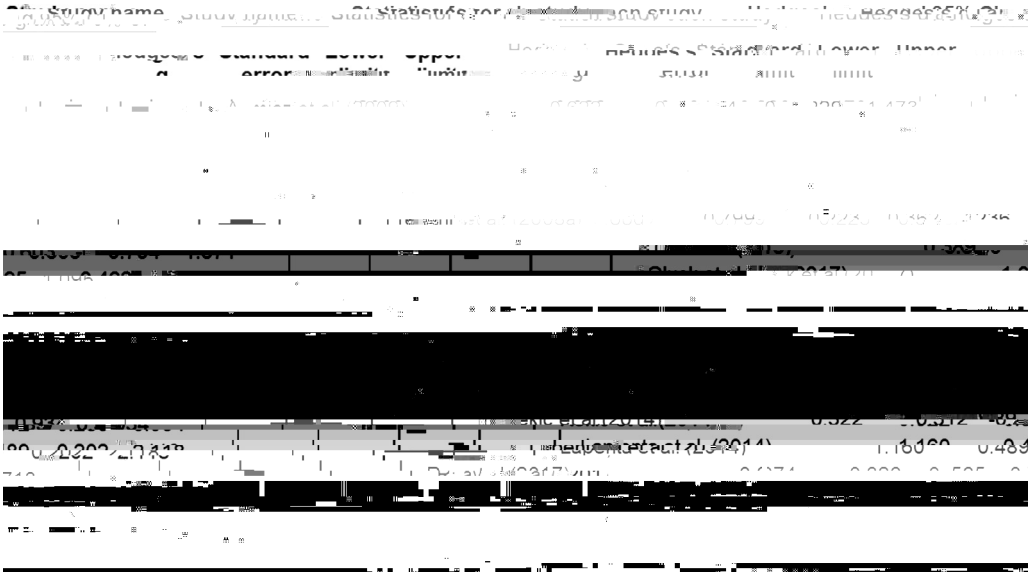

Fig. 6. The overall effect of neuromodulation on consumption.

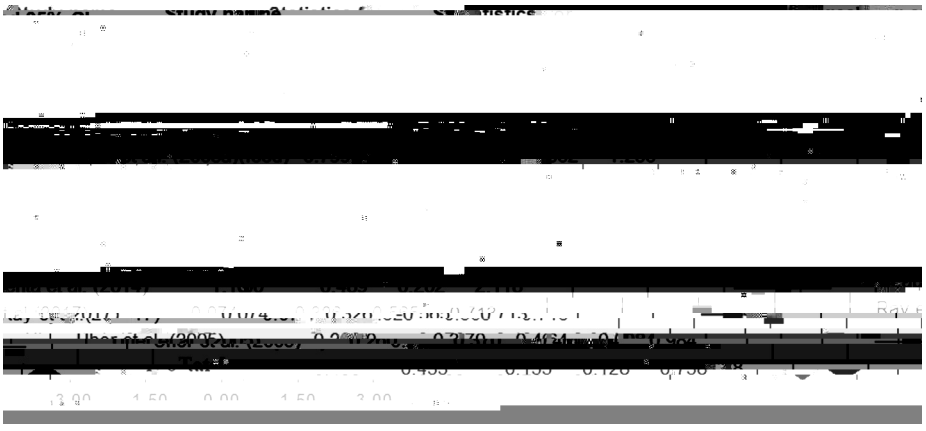

Fig. 7. The effect of single-session neuromodulation on consumption.

p < 0.0001) and a medium effect size for the reduction of food consumption (g = 0.560, CI: 0.279–0.841; z = 3.908, p < 0.0001). No study has investigated the effect of neuromodulation on consumption in individuals with alcohol or illicit drug addiction.

Comparing different stimulation techniques

The comparison of the two stimulation techniques (rTMS vs. tDCS) showed no significant differences in their overall

effectiveness for down-regulating craving ($Q = 0.307$, $p = 0.579$); with a significant effect for tDCS ($g = 0.490$, CI: 0.347−0.633; $z = 6.710$, $p < 0.0001$) and rTMS interventions ($g = 0.411$, CI: 0.170−0.651; $z = 3.350$, $p = 0.001$). When separately considering the effect on craving within single-session ($Q = 0.398$, $p = 0.528$) or multi-session interventions ($Q = 0.054$, $p = 0.816$), we also found no significant differences in the effectiveness between the two stimulation techniques. There were not enough studies to assess the session effect for consumption.

Comparing different stimulated hemispheres

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[63]