dysfunction. Over half the cohort demonstrated a significant decrease in depressive symptoms. Interestingly, two of the non-responders and one responder endorsed increased apathy despite stable or improving depressive symptoms, disinhibition, and executive dysfunction.
**Conclusions:** Surgical interventions for psychiatric disorders are emerging quickly and being refined daily. In this cohort, anterior capsulotomy via LITT provided full or partial OCD recovery for most patients. However, most patients reported significant increases in apathy, despite experiencing a decrease in depressive symptoms, with stable disinhibition and executive dysfunction. Despite these promising improvements in OCD symptomatology via LITT, impact of surgery on apathy levels is clearly warranted using objective, quantifiable methods. As apathy has consistently been related to functional impairment and poorer quality of life, understanding this outcome is imperative in larger trials. Better understanding of this finding and underlying circuity will allow patients to be fully informed regarding this promising surgical intervention.

**Categories:**
Neuropsychiatry/Psychopharmacology
**Keyword 1:** obsessive-compulsive disorder
**Keyword 2:** apathy
**Keyword 3:** treatment outcome
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## 62 Exploration of Sex Differences in Cannabis Use Patterns, Driving Performance, and Subjective Intoxication Effects

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**Objective:** Although some animal research suggests possible sex differences in response to THC exposure (e.g., Cooper & Craft, 2018), there are limited human studies. One study found that among individuals rarely using cannabis, when given similar amounts of oral and vaporized THC females report greater subjective intoxication compared to males (Sholler et al., 2020). However, in a study of daily users, females reported indistinguishable levels of intoxication compared to males after smoking similar amounts (Cooper & Haney, 2014), while males and females using 1-4x/week showed similar levels of intoxication, despite females having lower blood THC and metabolite concentrations (Matheson et al., 2020). It is important to elucidate sex differences in biological indicators of cannabis intoxication given potential driving/workplace implications as states increasingly legalize use. The current study examined if when closely matching males and females on cannabis use variables there are predictable sex differences in residual whole blood THC and metabolite concentrations, and THC/metabolites, subjective appraisals of intoxication, and driving performance following acute cannabis consumption.
**Participants and Methods:** The current study was part of a randomized clinical trial (Marcotte et al., 2022). Participants smoked *ad libitum* THC cigarettes and then completed driving simulations, blood draws, and subjective measures of intoxication. The main outcomes were the change in Composite Drive Score (CDS; global measure of driving performance) from baseline, whole blood THC, 11-OH-THC, and THC-COOH levels (ng/mL), and subjective ratings of how “high” participants felt (0 = not at all, 100 = extremely). For this analysis of participants receiving active THC, males were matched to females on 1) estimated THC exposure (g) in the last 6 months (24M, 24F) or 2) whole blood THC concentrations immediately post-smoking (23M, 23F).
**Results:** When matched on THC exposure in the past 6 months (overall mean of 46 grams; $p = .99$), there were no sex differences in any cannabinoid/metabolite concentrations at baseline (all $p > .83$) or after cannabis administration (all $p > .72$). Nor were there differences in the change in CDS from pre-to-post-smoking ($p = .26$) or subjective “highness” ratings ($p = .53$). When matched on whole blood THC concentrations immediately after smoking (mean of 34 ng/mL for both sexes, $p = .99$), no differences were found in CDS change from pre-to-post smoking ($p = .81$), THC metabolite concentrations (all $p > .25$), or subjective

https://doi.org/10.1017/S1355617723010482 Published online by Cambridge University Press

"highness" ratings (p = .56). For both analyses, males and females did not differ in BMI (both p > .7).
**Conclusions:** When male/female cannabis users are well-matched on use history, we find no significant differences in cannabinoid concentrations following a mean of 5 days of abstinence, suggesting that there are no clear biological differences in carryover residual effects. We also find no significant sex differences following *ad libitum* smoking in driving performance, subjective ratings of "highness," nor whole blood THC and metabolite concentrations, indicating that there are no biological differences in acute response to THC. This improves upon previous research by closely matching participants over a wider range of use intensity variables, although the small sample size precludes definitive conclusions.

**Categories:**
Neuropsychiatry/Psychopharmacology
**Keyword 1:** cannabis
**Keyword 2:** driving
**Keyword 3:** psychopharmacology
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## 63 Sex-Dependent Effects in Dopaminergic Modulation of Risky Decision-Making in Rats

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**Objective:** Determining neurobiological mechanisms underlying risk-taking behavior is paramount toward developing targeted therapeutics for psychiatric conditions with such behavioral deficits. Therapies are urgently needed given risk-taking is strongly linked to suicidal behavior. Risk-taking is often assessed in tasks of varied rewards and losses, complicating the interpretation of chasing rewards vs. avoiding punishments. A novel task in rats was designed which utilizes varying rewards only, so as to determine mechanisms contributing to 'chasing' higher rewards. This task was used to determine that the high reward (risk) preference of male rats was increased by pramipexole treatment [a dopamine D2 receptor-(D2R) family agonist] and decreased by optogenetic inhibition of D2R expressing neurons. The impact of D2R antagonists and sex-dependent differences were not examined however and remains unclear. Here, we trained female and male rats in the task to determine sex-differences in risk preference at baseline and in response to pharmacological challenges of pramipexole, the D2R antagonist sulpiride, and the dopamine transporter inhibitor GBR-12909.
**Participants and Methods:** In operant boxes animals could choose from one of two nose-pokes, one that delivered a 50 µl strawberry milkshake reward (safe-option), and the other a 10 µl reward with 75% probability and 170 µl reward with 25% probability (risky-option). Once trained to a stable baseline of risk preference, rats were treated with pramipexole (0.15- or 0.3-mg/kg; Experiment 1) or sulpiride (30-mg/kg; Experiment 2) for 3 days, each separated by a saline washout. Animals were once again trained to a stable baseline, then injected with GBR-12909 (5- or 16-mg/kg; Experiment 3)
**Results:** Baseline: females were less risk-adverse/more risk-prone than males.
Experiment 1: there was a main effect of drug on percent risk choice (%RC) change from baseline [$F(1,18)=10.5$, $p<0.01$], with pramipexole increasing %RC. When analyzed across each testing day, a main effect of session [$F(6,108)=3.6$, $p<0.005$] was observed, as was a session*sex*drug interaction [$F(6,108)=2.2$, $p<0.05$]. Post hoc analyses revealed females differed from males in the timing of their response to pramipexole based on dose.
Experiment 2: there was a main effect of drug on %RC change from baseline [$F(1,6)=20$, $p<0.01$], with sulpiride decreasing %RC. There was also evidence for a drug*sex interaction [$F(1,6)=3.6$, $p=0.11$], with more pronounced attenuation by sulpiride in females. A similar pattern was observed when analyzed across testing days.
Experiment 3: there was a main effect of drug on %RC change from baseline [$F(2,26)=4.0$, $p<0.05$], with the high dose of GBR-12909 (16-mg/kg) increasing %RC compared to VEH ($p<0.05$) and low dose (5-mg/kg).
**Conclusions:** Together these data indicate a sex-specific modulation of baseline risk preferences as measured explicitly via reward-

https://doi.org/10.1017/S1355617723010482 Published online by Cambridge University Press