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A meta-analysis of the sex-specific effects of psychotropic substances on acute striatal dopamine overflow measured by in vivo microdialysis in rats

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In recent years, the topic of sex differences has rightfully become a focus of scientific research. Current findings suggest sexual dimorphism in these neurophysiological brain pathways that are crucial for drug-seeking and addictive behavior, but how this affects the underlying neurochemical processes, is still widely unexplored.

Nevertheless, female subjects have been systemically ignored for decades in the field of microdialysis experiments and the few existing studies using female animals provide only small numbers. Moreover, there is increasing evidence that single preclinical studies often lack reproducibility. Therefore, a hypothesis-free meta-analysis approach was used that provides adequate statistical power for this subject area.

The main question of this thesis was whether data of microdialysis experiments indicate a difference in the dopaminergic overflow in reaction to drugs of abuse in male and female rats.

Thereby, systematic data mining was performed on the PubMed online library (<https://www.ncbi.nlm.nih.gov/pubmed/>) focusing on studies measuring extracellular dopamine concentrations in the striatal complex. The focused lied on six drugs of abuse (alcohol, amphetamine, cocaine, nicotine, morphine and tetrahydrocannabinol) and two brain regions (caudate putamen and nucleus accumbens).

Data from 45 microdialysis experiments on female rats (number of animals = 842) were extracted and statistically compared with data from 6402 male rats. Overall, 291 studies were included, providing averages of the peak percentage baseline value of dopamine for 103 different dosages.

All drugs under investigation notably increased the dopaminergic transmission in the striatal complex. For some drugs, a positive dose response relationship was detected. Regarding the entity of dose groups, no sex differences in the dopaminergic response to drugs of abuse were found, but for some small subgroups.

Neither did the rats' age, sex or state of consciousness have an impact on the overall peak percentage baseline values, suggesting robustness of these parameters. Attempts were also made to extract the rats' estrous cycle as a variable, but only one study monitored it.

Overall, the neglect of female subjects in basic research, which had lasted for decades and is far from defeated, was a phenomenon well reflected in the search query and the results of this thesis.

What can be therefore concluded, is that future research should intensify its efforts to include female subjects and to close the sex-gap in preclinical as well as in clinical research. This will provide more data that are crucial to get valid results about sex similarities or differences, as this thesis only shed light on a small subdivision.