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dSERT 1 MDRSGSSDFAGAAATTGRSNPAPWSDDKESPNNEDDSNEDD 41
dDAT  -----

dSERT 42 GDHTTPAKVTDPLAPKLANNERILVVSVTERTRETWGQKAE 82
dDAT  1 - -MSPTGHI SKSKTTPHDNDNNSISD - - - -ERETWSGKVD 35

dSERT 83 FLLAVIGFAVDLGNVWRFPYICYQNGGGAFLVPYCLFLIFG 123
dDAT  36 FLLSVIGFAVDLANVWRFPYLCYKNGGGAFLVPYGIMLVVG 76

dSERT 124 GLPLFYMELALGQFHRCCGLSIWKRICPALKGVGYAICLID 164
dDAT  77 GIPLFYMELALGQHNRKGAITCWGRLLVPLFKGIGYAVVLLIA 117

dSERT 165 IYMGMYNYNTIIGWAVYYL FASFTSKLPWTSCDNPWNTENCM 205
dDAT  118 FYVDFYYNVI IAWSLRFF FASFTNSLPWTSCNNI WNTPNCR 158

dSERT 206 QVTSENFTELAT - - - - - 217
dDAT  159 PFESQNASRVPVIGNYSDLYAMGNQSLLYNETYMNGSSLDT 199

dSERT 218 - - - - - SPAKEFFERKVL ESYKGNGLDFMGPVKPTLA 248
dDAT  200 SAVGHVEGFQSAASEYFNRYI LELNRSEGIHDLGAIKWDM 240

dSERT 249 LCVFGVFVLVYFSLWKG VRSAGKVWWTALAPYVVL ILLV 289
dDAT  241 LCLLIYVLYICYFSLWKGISTSGKVWWTALFPYAVLLILLI 281

dSERT 290 RGVSLPGADEGIKYLTPEWHKLKNSKVWIDAASQIFFSLG 330
dDAT  282 RGLTLPGSFLGIQYLTNPFSAIYKAEVWVDAATQVFFSLG 322

dSERT 331 PGFGTLLALSSYNKFNNNCYRDALITSSINCLTSFLAGFVI 371
dDAT  323 PGFGVLLAYASYNKYHNNVYKDALLTSFINSATSEIAGFVI 363

dSERT 372 FSVLGYMAYVQKTSIDKVGLEGPGLVFI VYPEAIATMSGSV 412
dDAT  364 FSVLGYMAHTLGVRIEDVATEGPGLVFVYPAAIATMPAST 404

dSERT 413 FWSIIFFLMLITLGLDSTFGGLEAMITALCDEYPRVIGRRR 453
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dSERT 454 ELFVLLLLAFIFLCALPTMTYGGVVLVNFNVYGPGLAILF 494
dDAT  445 ELFVAGLFSLYFVVG LASCTQGGFYFFHLLDRYAAGYSILV 485

dSERT 495 VVFVEAAGVWFYGVDRFSSDVEQMLGSKPGLFWRICWTYI 535
dDAT  486 AVFFEAIAVSWIYGTNRFSEDI RDMIGFPGRYWQVCWRFV 526

dSERT 536 SPVFLLTIFIFSIMGYKEMLGEEYYPDWSYQVGVAVTCSS 576
dDAT  527 APIFLLFITVYGLIGYEPLTYADVYPSWANALGWC IAGSS 567

dSERT 577 VLCIPMYIIYKFFFAKGGCRQRLQESFQPEDNCGSVVPGQ 617
dDAT  568 VVMIPAVAIIFKLL-STPGSLRQRF TILTPWRDQQSMAMVL 607

dSERT 618 QGTSV - - - - - 622
dDAT  608 NGVTTEVTVVRLTDTETAKEPVDV 631

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Figure S1: Sequence alignment of dSERT and dDAT using Jalview 2.8.1. Conserved amino acid residues are indicated in blue box.

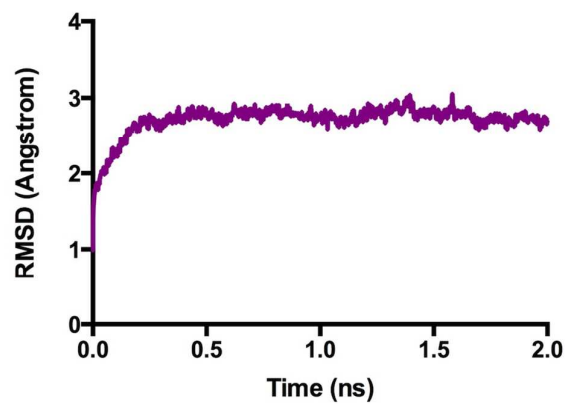


Figure S2: The Root Mean Square Deviations (RMSD) of backbone atoms relative to the starting complex dSERT/4-MTA during the 20 ns molecular dynamics.

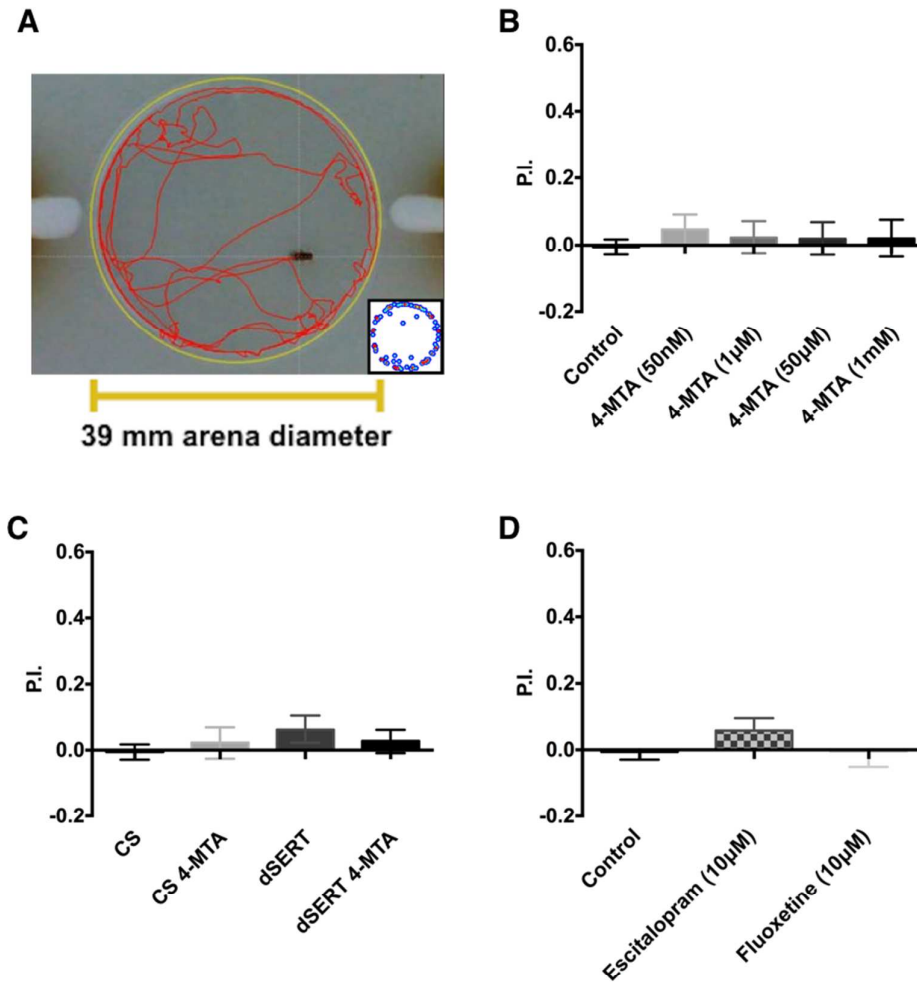


Figure S3: In absence of odorant, flies do not express preference for any side of the arena. (A) Set up for behavioral assay. It is possible to track the movement of fly in a circular arena (red traces). In the representative experiment shown, it is not possible to detect a preference of the fly for a side (left or right). (B) Flies exposed to different concentration of 4-MTA do not show preference for any side in the arena. (C) Control of dSERT mutant flies, fed or not with 4-MTA, show no naïve preference for a side of the arena. The number of experiments (“n”) in (B) and (C), in each condition, is as indicated in Fig. 5. (D) Flies show no preference for any side of the arena, even

when fed drugs that act on dSERT (10 μ M escitalopram and 10 μ M fluoxetine). The number of experiments (“n”) per condition is 21, 12 and 15 flies, respectively.

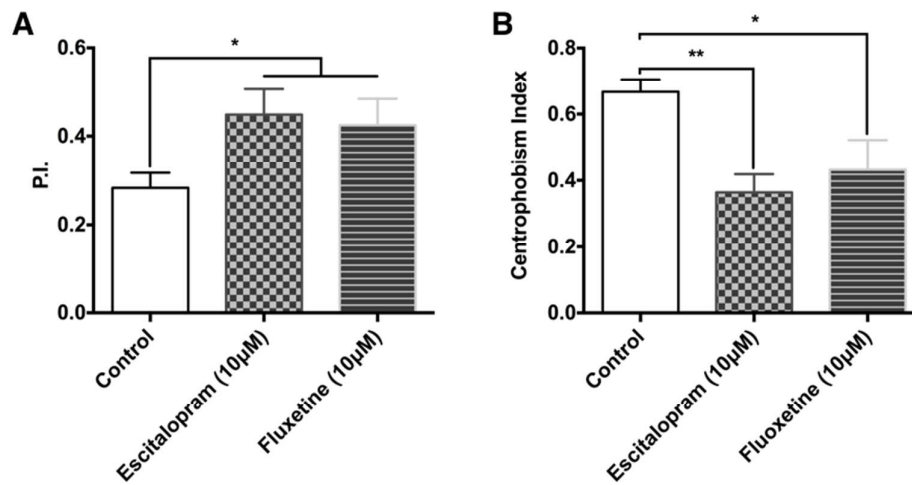


Figure S4: Feeding control flies with escitalopram or fluoxetine affects olfactory response and centrophobism. (A) Aversive response towards Bz, measured as Performance Index (P.I.) is significantly increased after feeding flies escitalopram (10 μ M) or fluoxetine (10 μ M). One-way ANOVA followed by Tukey post-test; * indicates $p < 0.05$ as compared to control situation (no drug) (B) Centrophobism is decreased after flies are fed escitalopram (10 μ M) or fluoxetine (10 μ M) for five minutes. One-way ANOVA followed by Tukey post-test; * indicates $p < 0.05$ as compared to control situation (no drug). The number of experiments (“n”) per condition is 21, 12 and 15 flies, respectively.

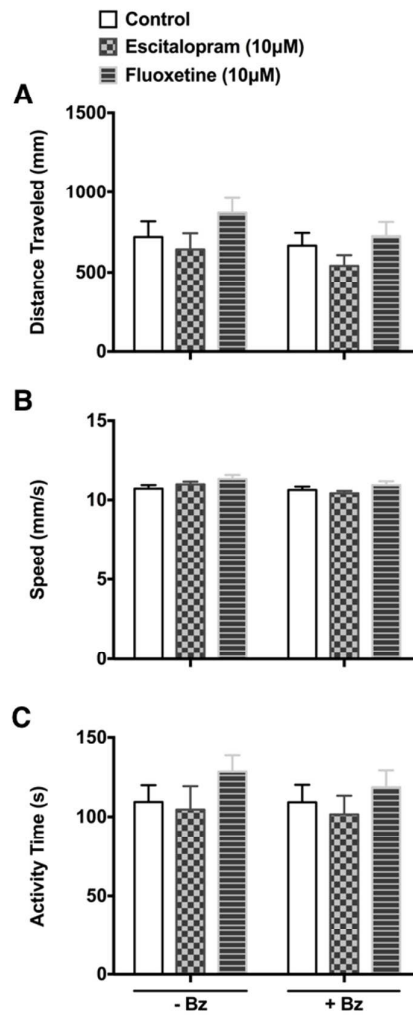


Figure S5: Feeding control flies escitalopram or fluoxetine does not affect motor performance. Flies were fed escitalopram (10 μ M) or fluoxetine (10 μ M) for five minutes. Afterwards, three parameters were assessed: (A) Distance traveled, (B) Speed and (C) Activity time. No statistical differences were observed between the experimental groups. One-way-ANOVA followed by Tukey post-test. The number of experiments (“n”) per condition is 21, 12 and 15 flies, respectively.