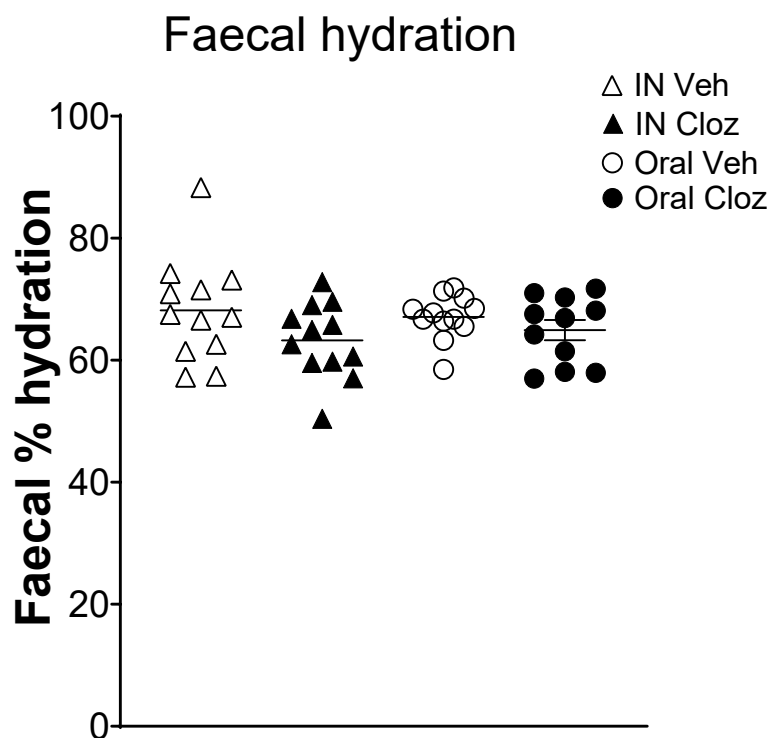


Supplementary Table 1. Animal stratification based on performance across behavioural tests.

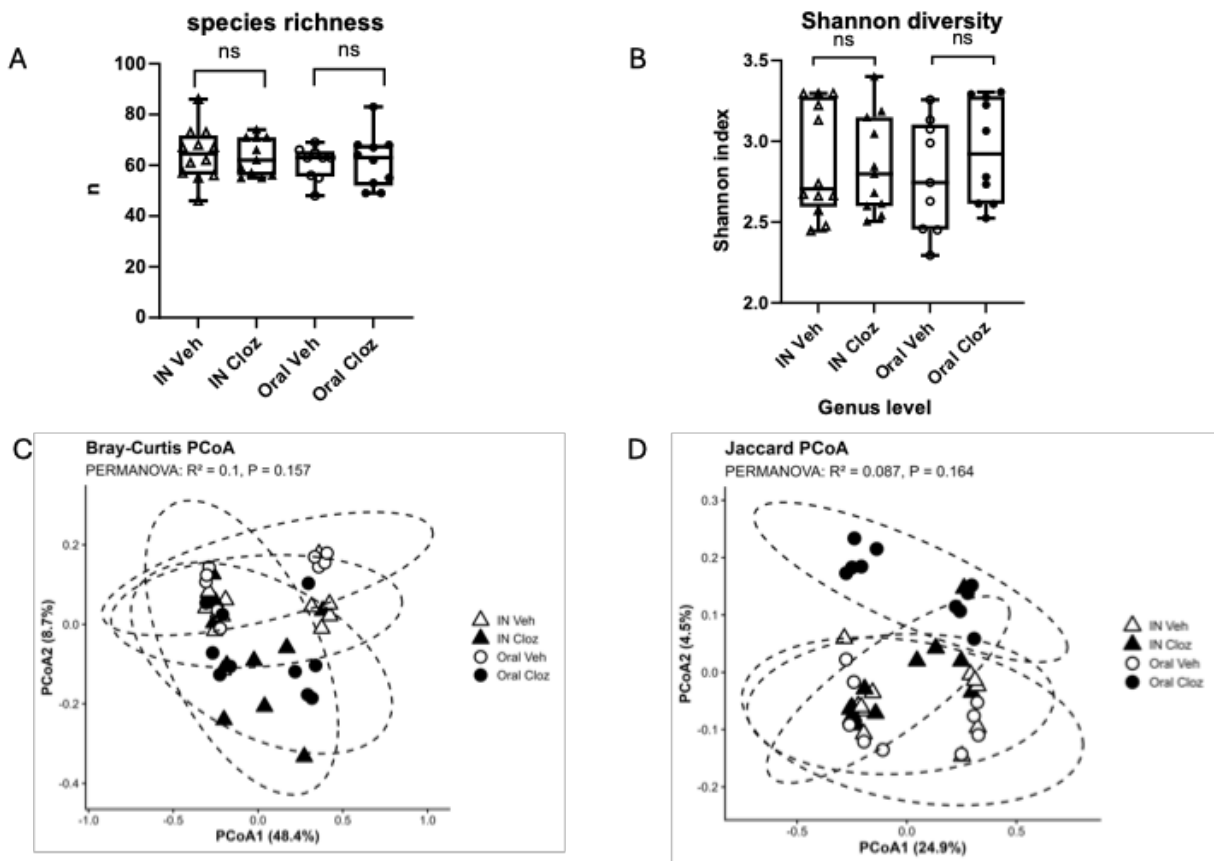
Animal ID	PPI score	Amph- Loco score	CAR score	Individual total score	Box score	Treatment
1	2	2	4	8	33	IN Veh
2	4	1	4	9		
3	1	3	4	8		
4	2	2	4	8		
5	1	3	4	8	34	IN Veh
6	2	4	4	10		
7	2	3	4	9		
8	2	1	4	7		
9	2	2	4	8	31	IN Veh
10	2	3	1	6		
11	2	3	4	9		
12	2	2	4	8		
13	2	1	4	7	33	IN Cloz
14	2	4	4	10		
15	2	2	3	7		
16	2	3	4	9		
17	2	2	4	8	29	IN Cloz
18	2	4	2	8		
19	1	3	1	5		
20	1	3	4	8		
21	1	2	4	7	28	IN Cloz
22	2	2	1	5		
23	3	3	4	10		
24	2	1	3	6		
25	2	2	4	8	31	Oral Veh
26	2	3	4	9		
27	1	3	4	8		
28	2	3	1	6		
29	2	4	4	10	34	Oral Veh
30	2	3	4	9		
31	2	3	4	9		
32	2	2	2	6		
33	3	3	1	7	30	Oral Veh
34	1	3	3	7		
35	3	2	4	9		
36	2	2	3	7		
37	3	3	4	10	33	Oral Cloz
38	2	3	2	7		
39	2	2	4	8		
40	2	2	4	8		

41	1	2	4	7	26	Oral Cloz
42	2	3	4	9		
43	1	2	0	3		
44	2	3	2	7		
45	2	4	4	10	36	Oral Cloz
46	3	2	4	9		
47	1	3	4	8		
48	2	3	4	9		

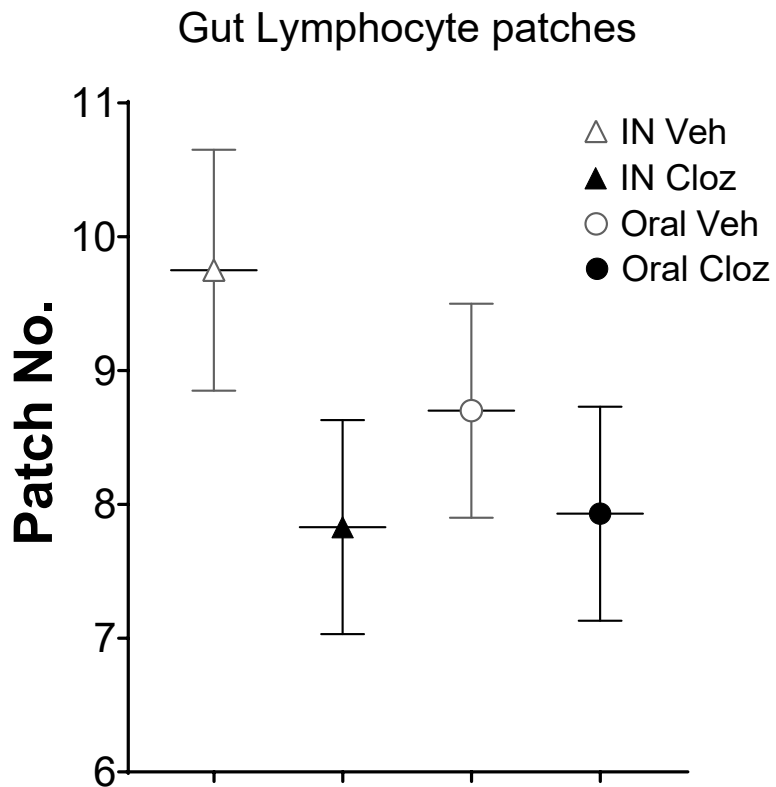
Abbreviations: PPI, prepulse inhibition; Amph-Loco, amphetamine-induced locomotor activity; CAR, conditioned avoidance response. Animals were stratified according to their combined performance across behavioural tests, with the individual total score used to determine group allocation.



Supplementary Figure 1. Clozapine does not affect faecal hydration. No significant differences in the hydration state of rat faecal boli were observed following clozapine treatment, indicating no evidence of constipation.



Supplementary Figure 2. Alpha and beta diversity analyses of the gut microbiota across the four study groups. No significant differences were observed in alpha diversity, as assessed by species richness (A) and the Shannon index (B), among the four groups. Similarly, no significant differences were detected in beta diversity, as assessed by the Jaccard index (C) and Bray–Curtis dissimilarity (D), among the four groups.



Supplementary Figure 3. Clozapine does not alter gut lymphocyte aggregates. No significant differences in gut lymphocyte aggregates were observed following clozapine treatment, irrespective of the route of administration. Data are presented as mean $\pm$ SEM ($n = 9\text{--}12$ per group). IN, intranasal; Cloz, clozapine; Veh, vehicle.