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Sodium nitroprusside as an adjunctive treatment for schizophrenia reduces Ndel1 oligopeptidase activity – Nani JV et al.

Table S1 Description of the experimental protocol

Time	Procedure
Enrollment	- Routine assessments in the psychiatric ward at HCFMRP-USP
	- Screening and diagnosis (SCID-IV)
Monthly trial session	
T0 (baseline)	- Start of monitoring HR, BP and O_2 saturation
	- Venous puncture
	- Clinical evaluation: BPRS, PANSS and UKU
Start of infusion (sNP or PLC)	
T1 (60 min)	- Clinical evaluation: BPRS, PANSS
T2 (120 min)	- Clinical evaluation: BPRS, PANSS
T3 (180 min)	- Clinical evaluation BPRS, PANSS
T4 (240 min)	- Clinical evaluation: BPRS, PANSS
End of infusion	
End of eight experimental sessions	
Reassessment after 15 days	- Clinical evaluation: BPRS, PANSS, UKU
Reassessment after 30 days	- Clinical evaluation: BPRS, PANSS, UKU
Reassessment after 60 days	- Clinical evaluation: BPRS, PANSS, UKU

BP = blood pressure; BPRS = Brief Psychiatric Rating Scale; HCFMRP-USP = Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo; HR = heart rate; PANSS = Positive and Negative Syndrome Scale; PLC = placebo; SCID-IV = Structured Clinical Interview for DSM-IV; sNP = sodium nitroprusside; UKU = Udvalg for Kliniske Undersøgelser.

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Table S2 Clinical characteristics of patients in groups I and II, before (baseline, t = 0) and 4 h after (t = 4) each infusion of placebo or sodium nitroprusside in the first treatment round, namely phase A, comprising four infusions of 4 h each followed by 1-month intervals

	Schizophrenia (n=15)								Comparative analysis between groups at baseline	
	Group I (n=7)				Group II (n=8)					
	t = 0 (before)	t = 4 (after)	Test value	p-value	t = 0 (before)	t = 4 (after)	Test value	p-value	Test value	p-value
PANSS										
Positive	9.9 (3.3)	7.7 (0.9)	4.273	<0.001*	16.3 (4.0)	10.1 (2.3)	10.53	<0.001*	7.056	<0.001*
Negative	22.7 (4.3)	20.7 (4.2)	4.356	<0.001*	19.9 (7.1)	15.9 (6.0)	8.261	<0.001*	1.654	0.103
BPRS	12.2 (3.6)	6.6 (3.1)	9.353	<0.001*	15.8 (5.7)	7.3 (2.9)	10.631	<0.001*	2.811	0.006

BPRS = Brief Psychiatric Rating Scale; PANSS = Positive and Negative Syndrome Scale.
* Statistical significance was defined as $p \leq 0.05$.

Table S3 Clinical characteristics of patients in groups I and II before (baseline, t = 0) and 4 h after (t = 4) infusion of placebo or sodium nitroprusside in the second round of treatment, namely phase B, comprising four infusions of 4 h each followed by one-month intervals

	Schizophrenia (n=15)								Comparative analysis between groups at baseline	
	Group II (n=8)				Group I (n=7)					
	t = 0 (before)	t = 4 (after)	Test value	p-value	t = 0 (before)	t = 4 (after)	Test value	p-value	Test value	p-value
PANSS										
Positive	15.2 (3.6)	14.6 (3.1)	1.958	0.059	14.9 (5.3)	14.8 (5.2)	0.372	0.712	0.195	0.846
Negative	19.3 (7.0)	19.2 (6.9)	0.387	0.701	25.5 (5.3)	24.4 (6.1)	2.143	0.040	3.940	<0.001*
BPRS	13.6 (3.1)	13.1 (3.1)	1.438	0.160	17.3 (5.0)	16.1 (5.3)	4.518	<0.001*	4.237	<0.001*

BPRS = Brief Psychiatric Rating Scale; PANSS = Positive and Negative Syndrome Scale.
* Statistical significance was defined as $p \leq 0.05$.

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Table S4 Cardiovascular characteristics of patients in groups I and II before (at baseline, t = 0) and 4 h after (t = 4) each infusion of placebo or sodium nitroprusside in the first and second treatment round, namely phase A and B

Treatment/ cardiovascular parameters	Schizophrenia (n=15)								Comparative analysis between groups at baseline	
	Group I (n=7)				Group II (n=8)					
	t = 0	t = 4	Test value	p-value	t = 0	t = 4	Test value	p-value	Test value	*p*-value
Phase A										
sBP	125.2 (16.2)	114.5 (16.5)	4.996	<0.001*	124.5 (14.8)	112.5 (11.3)	4.895	<0.001*	0.171	0.864
dBP	68.6 (10.5)	61.45 (13.9)	3.529	0.001*	65.3 (8.3)	57.8 (8.9)	3.046	0.004*	1.126	0.212
HR	96.6 (15.2)	104.1 (14.7)	3.113	0.004*	92.5 (12.4)	96.6 (13.0)	1.853	0.073	1.109	0.272
	Group II (n=8)				Group I (n=7)					
Phase B										
sBP	125.5 (16.2)	127.9 (16.5)	0.939	0.355	124.5 (13.4)	123.8 (12.6)	0.259	0.797	0.287	0.774
dBP	69.1 (8.6)	70.4 (10.3)	0.659	0.514	69.2 (11.1)	69.1 (8.9)	0.013	0.989	0.035	0.972
HR	89.7 (10.2)	88.4 (10.7)	0.930	0.359	91.9 (14.3)	98.1 (13.4)	2.174	0.038*	0.684	0.496

Data presented as mean (SD), unless otherwise specified.
dBP = diastolic blood pressure; HR = heart rate; sBP = systolic blood pressure.
* Statistical significance was defined as $p \leq 0.05$.

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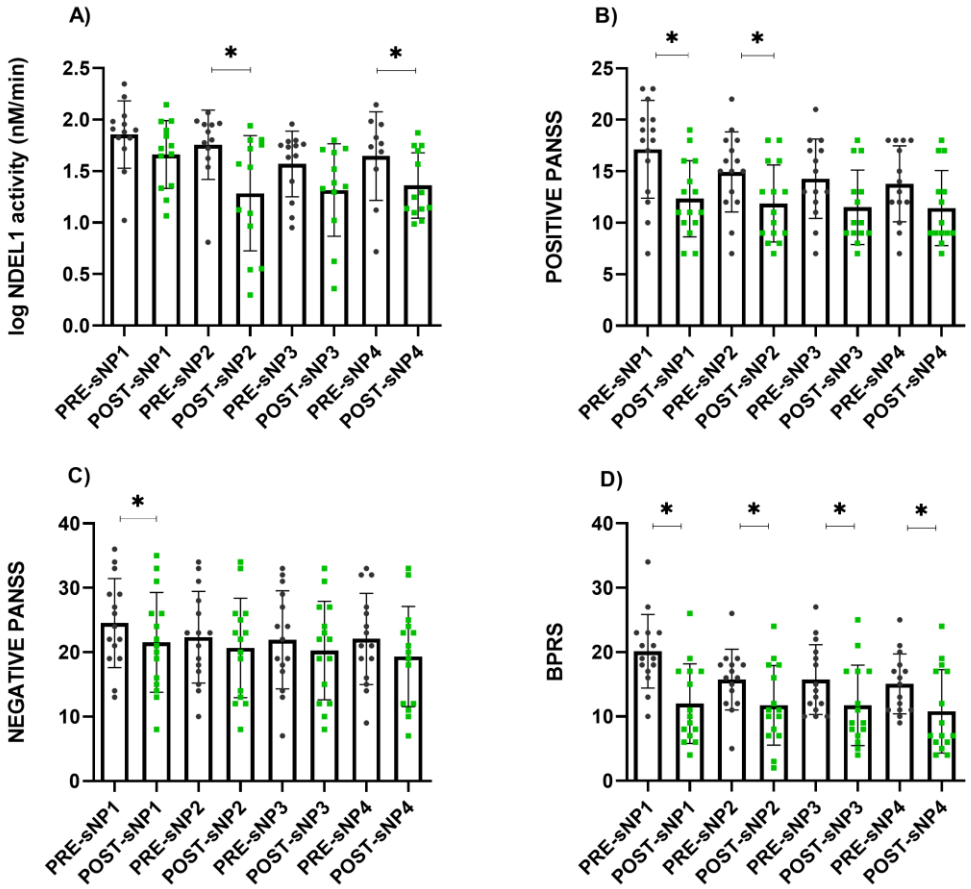
Figure S1 Values of A) log Ndel1 activity, B) positive and c) negative PANSS, and D) BPRS for patients in group I and group II before and after each sNP treatment session



Values represent the four infusion sessions (each session is indicated in the X-axis as sNP1, sNP2, sNP3, and sNP4) of sNP for each patient with schizophrenia, with Ndel1 activity and clinical aspects assessed before and 4 h after infusion. Paired t-test, * $p \leq 0.05$. BPRS = Brief Psychiatric Rating Scale; Ndel1 = nuclear distribution element-like 1; PANSS = Positive and Negative Syndrome Scale; sNP = sodium nitroprusside.

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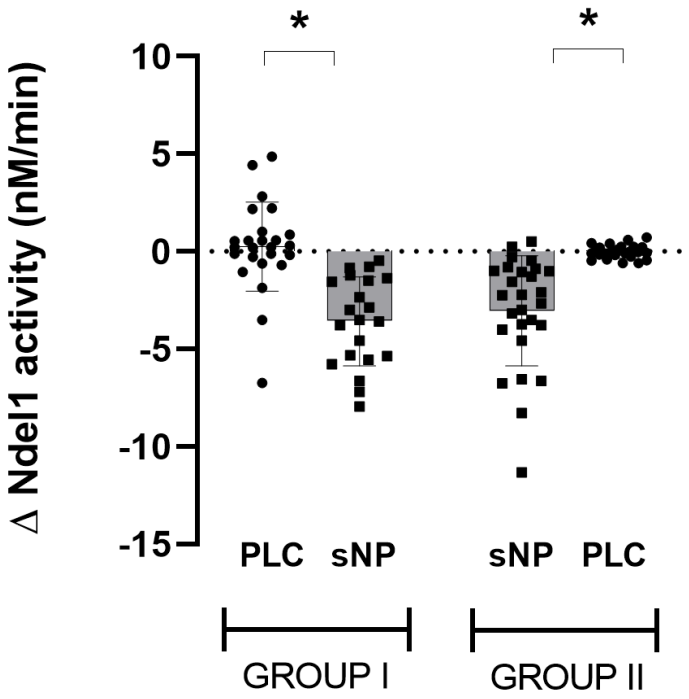
Figure S2 Delta Ndel1 activity in serum of patients with schizophrenia treated with PLC or sNP



The Ndel1 activity was measured in the serum of all patients with chronic schizophrenia (N = 15) just before (baseline) and 4 h after they have received PLC or sNP infusion. The present data correspond to the △Ndel1 activity (μM/min) for each double blind-randomized group, namely group I (n=7, placebo first) and group II (n=8, sNP first). The statistical analysis employed paired t-test, * $p \leq 0.05$ for the comparison of the values differences observed after the infusion of PLC or sNP minus their respective baseline value. Ndel1 = nuclear distribution element-like 1; PLC = placebo; sNP = sodium nitroprusside.