Mitochondrial DNA copy number is associated with psychosis severity and anti-psychotic treatment.

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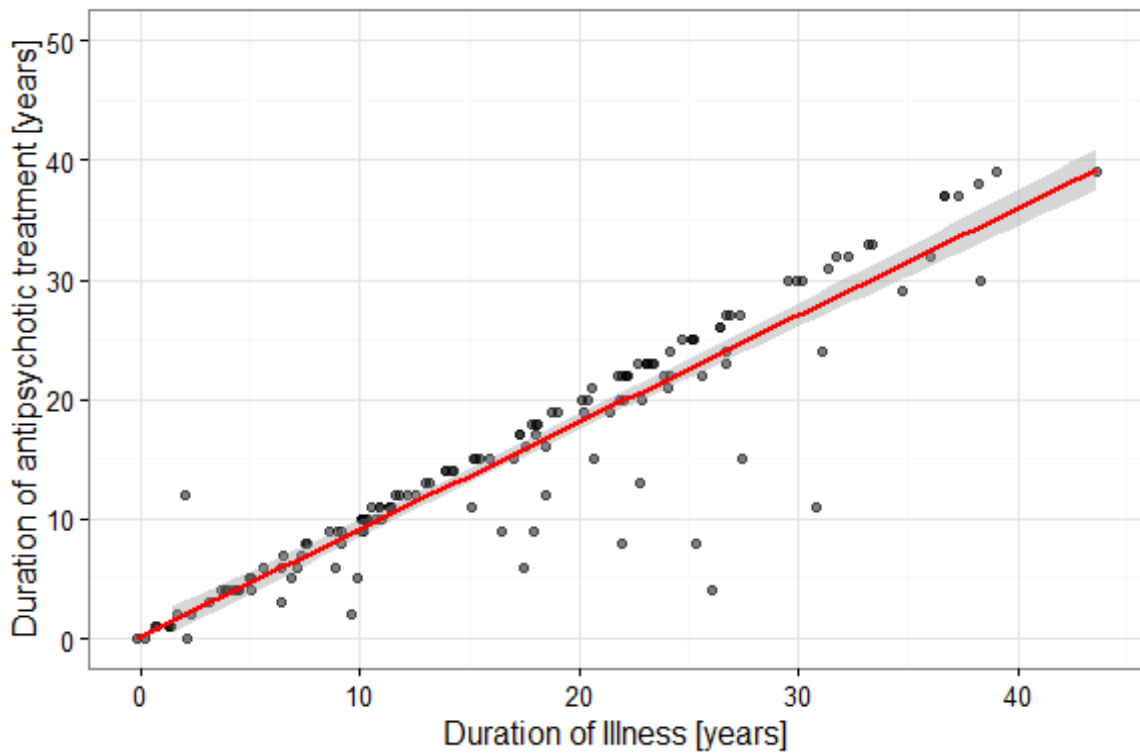parvin.kumar@ki.se; Tel: +46-8-51776524; Fax: +46-8-51773909

Figure S1A: Duration of antipsychotic treatment positively correlated with duration of illness within the cohort of patients on clozapine and risperidone (Spearman's $\rho = 0.915$, $p < 0.001$, n = 145).
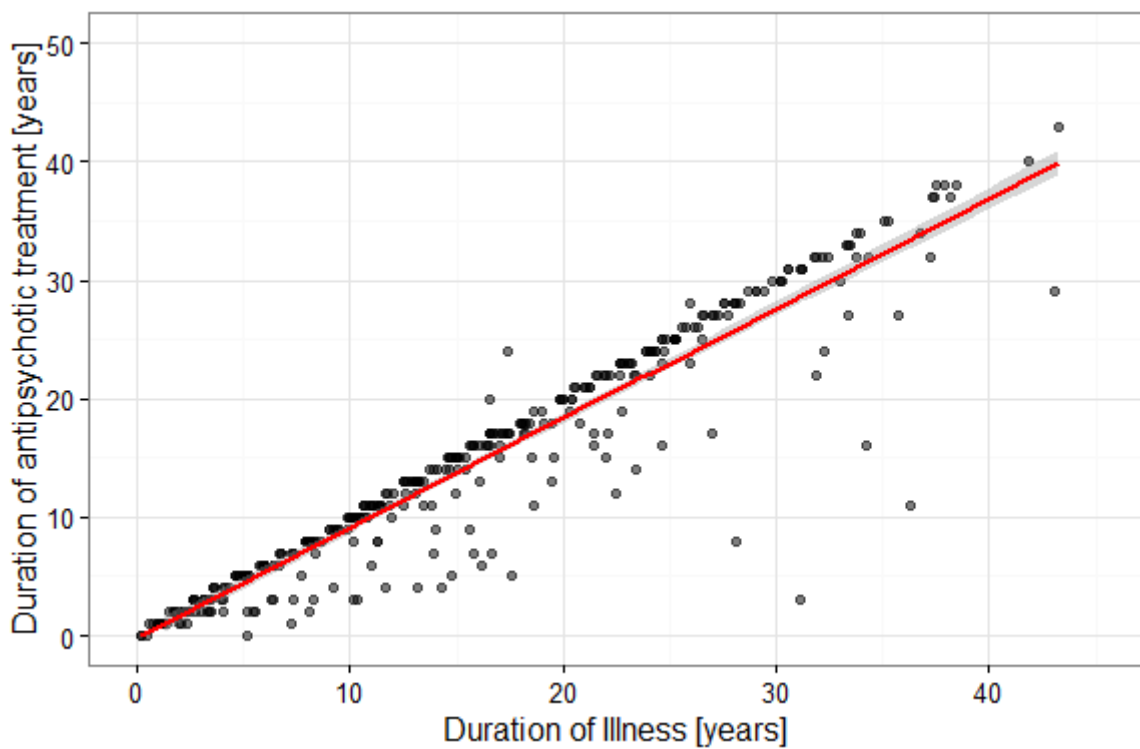

Figure S1B: Duration of antipsychotic treatment positively correlated with duration of illness within the cohort of patients not on clozapine and risperidone (Spearman's $\rho = 0.944$, $p < 0.001$, n = 359).
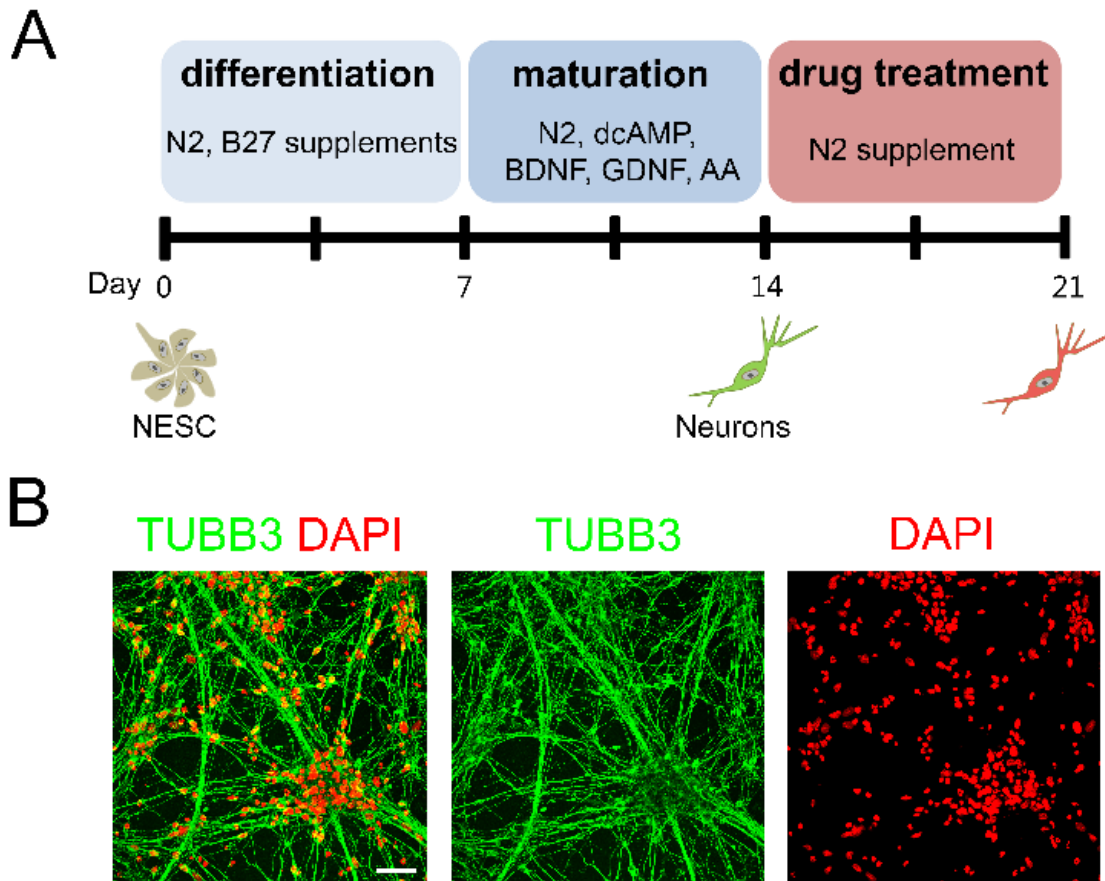
Figure S2A and S2B

In vitro effects of anti-psychotics on mitochondrial DNA copy number in neurons derived from human neuroepithelial stem cells (NESCs).

(A) NESCs were differentiated for 7 days with N2 and B27. They were matured with N2, dcAMP, brain-derived neurotrophic factor (BDNF), glial cell-derived neurotrophic factor (GDNF) and ascorbic acid (AA). (B) Mature neurons' morphology was characterized through stains for neuronal marker TUBB3, white scale bar: 50 μm.
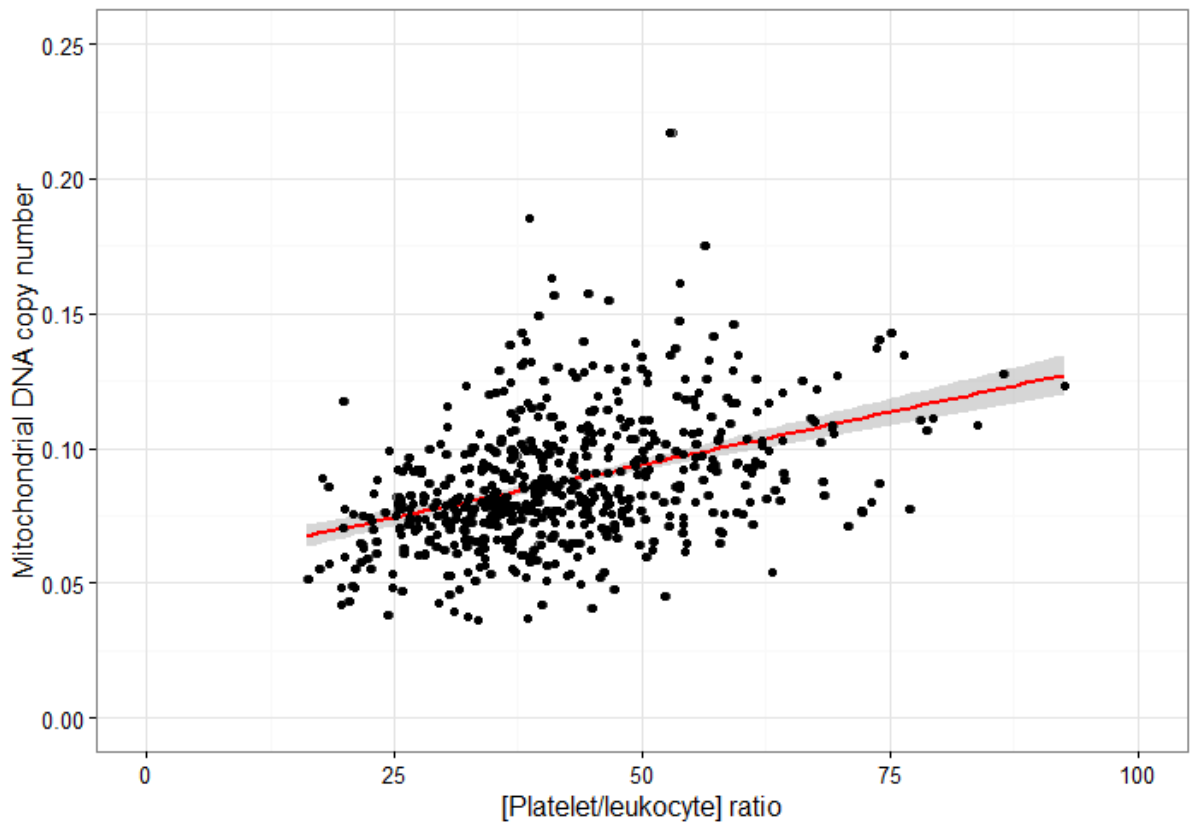
Figure S3: Whole blood mtDNA copy number was associated with the platelet to leukocyte count ratio (ρ = 0.422, p=2.2e-16). Therefore, mtDNA copy number was regressed on [platelet/leukocyte] ratio to obtain normally distributed unstandardized residuals. The residual variable designated mtDNAcn$_{res}$ represents the variance of whole blood mtDNA copy number that is unbiased by platelet to leukocyte count.

Figure S4A: Proportion of life on antipsychotic treatment positively correlated with Clinical Global Impression CGI (score) within the group of patients on treatment with clozapine and risperidone (Spearman's $\rho = 0.258$ p $= 0.002$, n $= 140$ and $\beta = 0.248$).
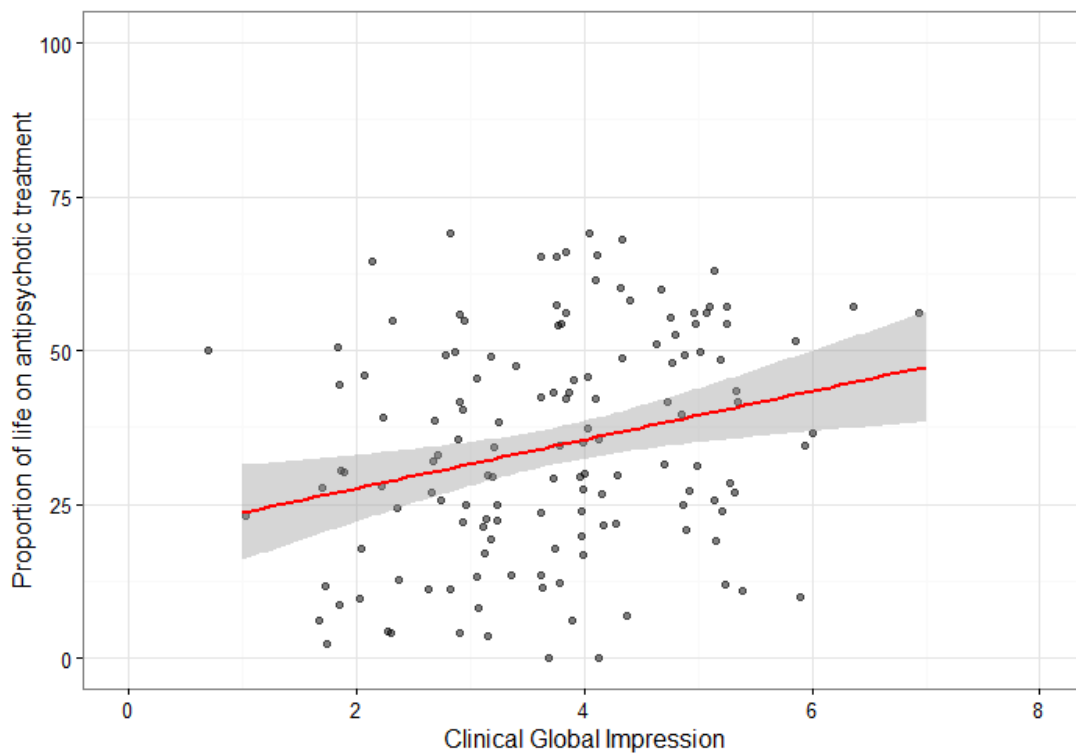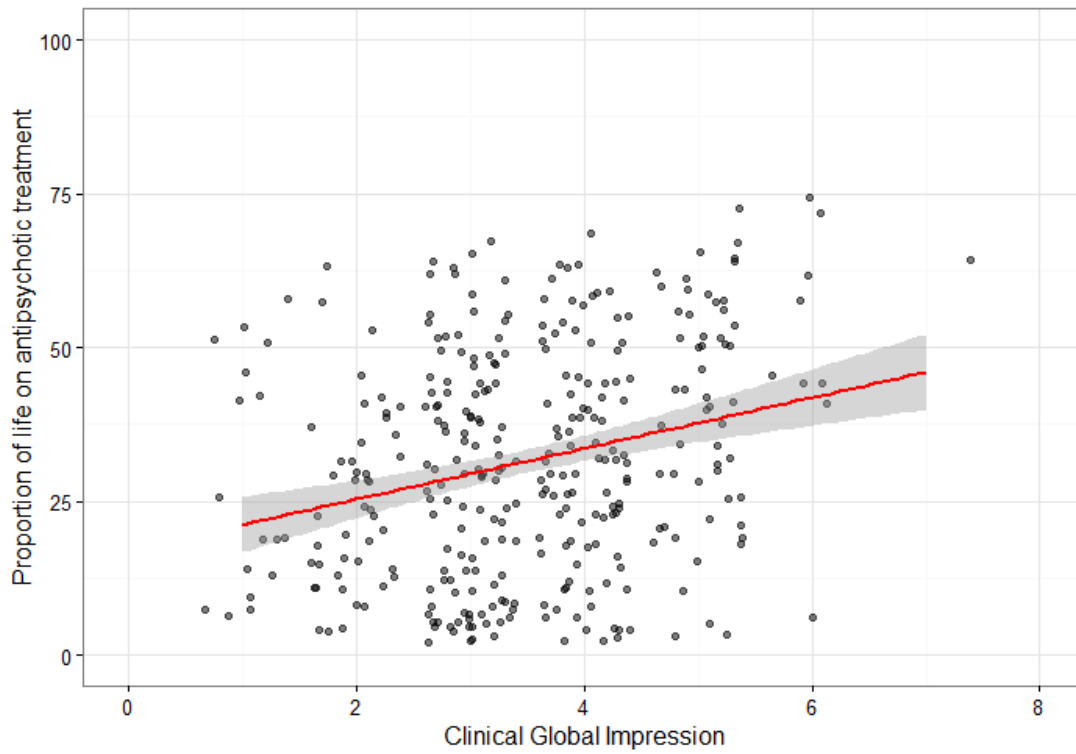
Figure S4B: Proportion of life on antipsychotic treatment positively correlated with Clinical Global Impression CGI (score) within the group of patients not on clozapine and risperidone treatment (Spearman's ρ = 0.234, p <0.001, n = 349 and β=0.251)

Table S1: Final models of clinical parameters associated with whole blood mitochondrial DNA copy number adjusted for platelet to leukocyte count. Analyses restricted to patients with Schizophrenia diagnosis, N=306.

Variable	B	SE	$\beta_{standardized}$	t	p
Model 1 : Clinical profile (adjusted R^2 = 0.031, ANOVA: F= 5.65 , n =288)					
(Constant)	0.117	0.010		12.2	<0.001
Age	<0.001	<0.001	-0.120	-2.071	0.039
CGI	-0.004	0.001	-0.145	-2.495	0.013
Model 2 : Treatment (adjusted R^2 = 0.052, ANOVA: F = 5.65, n = 279)					
(Constant)	0.114	0.009		13.1	<0.001
Age	-0.001	<0.001	0.170	-2.87	0.004
Clozapine	-0.013	0.005	-0.172	-2.89	0.004
Risperidone	-0.010	0.004	-0.139	-2.37	0.019
Model 3 Group A : Treatment vs psychosis severity (adjusted R^2 = 0.040 , ANOVA: F = 5.02, n = 96)					
(Constant)	0.088	0.055		19.1	<0.001
Proportion of life on treatment	-0.001	<0.001	-0.224	-2.24	0.027
Model 3 Group B : Treatment vs psychosis severity (adjusted R^2 = 0.018 , ANOVA: F = 4.39, n = 190)					
(Constant)	0.106	0.008		13.9	<0.001
CGI	0.004	0.002	-0.151	-2.10	0.037
Model 4 Group A : Metabolic profile (adjusted R^2 = 0.049, ANOVA: F = 5.37 , n = 85)					
Proportion of life on treatment	-0.001	<0.001	-0.245	-2.32	0.023
Model 4 Group B : Metabolic profile (n = 204)					
No significant predictors					

CGI: Clinical Global Impression-Severity

Group A: patients receiving clozapine or risperidone

Group B: patients not receiving clozapine or risperidone