

**Supplementary Material to MS 275937**

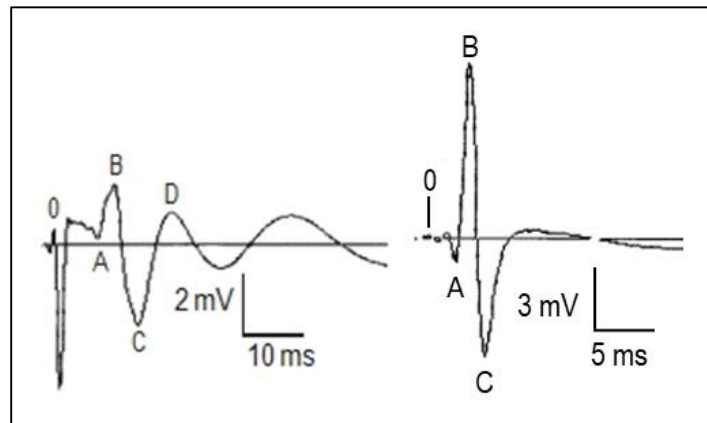
**Supplementary Table 1** Organ weights related to 1/100 body weight in the control and treated animals.

<b>Groups</b>	<b>Lungs</b>	<b>Kidneys</b>	<b>Brain (complete)</b>	<b>Liver</b>
<i>C</i>	0.501 ± 0.201	0.723 ± 0.082	0.491 ± 0.044	3.231 ± 0.326
<i>VT</i>	0.607 ± 0.256	0.703 ± 0.082	0.498 ± 0.037	2.663 ± 0.148
<i>LD</i>	0.687 ± 0.148	0.804 ± 0.136	0.501 ± 0.027	3.173 ± 0.500
<i>MD</i>	0.755 ± 0.235	0.793 ± 0.101	0.498 ± 0.027	3.271 ± 0.688 #
<i>HD</i>	0.863 ± 0.105***#	0.927 ± 0.093*#	0.497 ± 0.025	3.916 ± 0.520 ***oo&

**Notes:** Means±SD; n=10. \*, \*\*: p<0.05, 0.01 vs *C*; ##, ###: p<0.01, 0.001 vs. *VT*; oo: p<0.01 vs *LD*; &: p<0.05 vs *MD*.

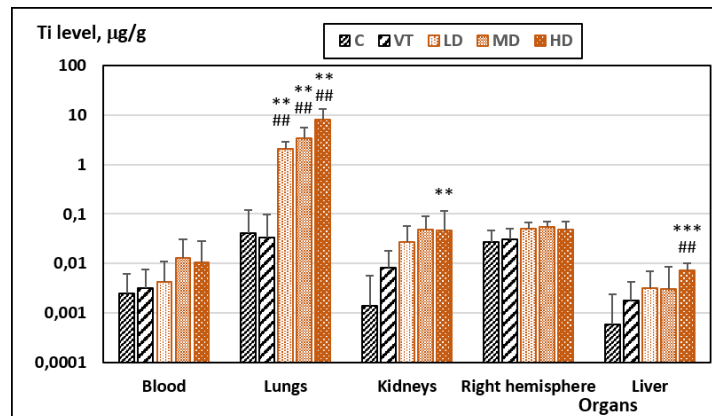
**Abbreviations:** *C*, control; *VT*, vehicle treated; *LD*, low dose treated; *MD*, medium dose treated; *HD*, high dose treated.

## Supplementary figures



**Supplementary Figure 1** Samples of recorded electrical activity. Left, somatosensory evoked potential; right, tail nerve compound action potential.

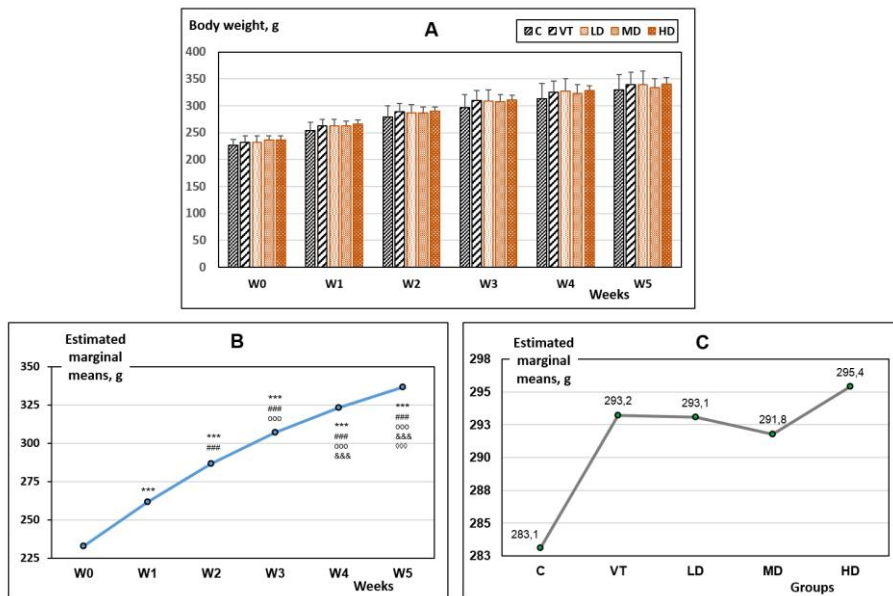
**Notes:** Onset latency of both forms of evoked activity was measured between stimulus artifact (point marked 0) and point A. Peak-to-peak amplitude of the somatosensory evoked potential was measured between points B and C.



**Supplementary Figure 2** Levels of chemically detected Ti in tissue samples of control and treated rats.

**Notes:** Means+SD, n=10. \*\*, \*\*\*: p<0.01, 0.001 vs C; ##: p<0.01 vs VT.

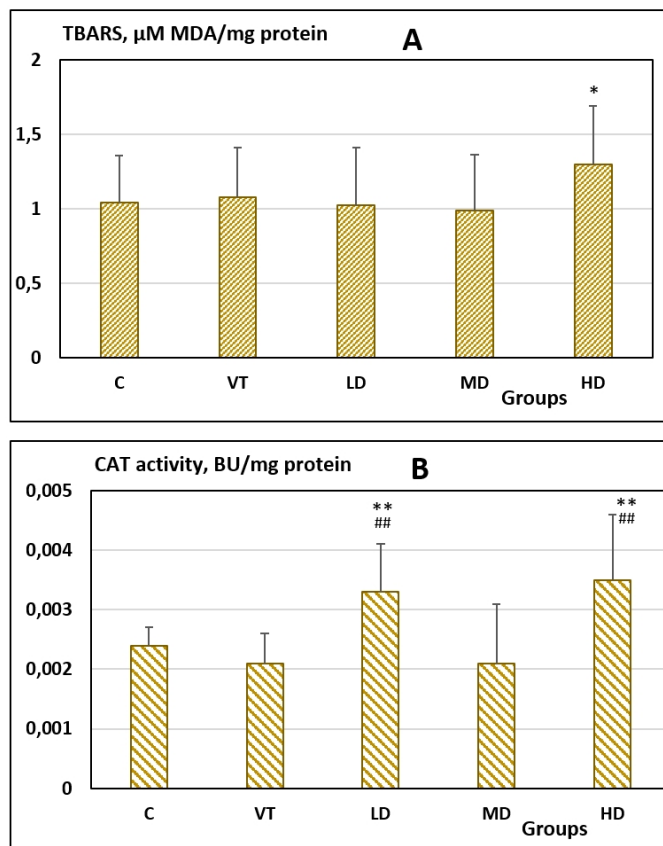
**Abbreviations:** C, control; VT, vehicle treated; LD, low dose treated; MD, medium dose treated; HD, high dose treated.



**Supplementary Figure 3** Body weight of the control and treated rats during the 6 weeks of the experiment. **A**, weekly weight data (Means+SD, n=10). **B** and **C**, result of statistical analysis (GLM) of the effect of treatment time (**B**) and dose (**C**) on body weights.

**Notes:** \*\*\*: p<0.001 vs. C; ###: p<0.001 vs. VT; ooo: p<0.001 vs. LD; &&&: p<0.001 vs. MD.

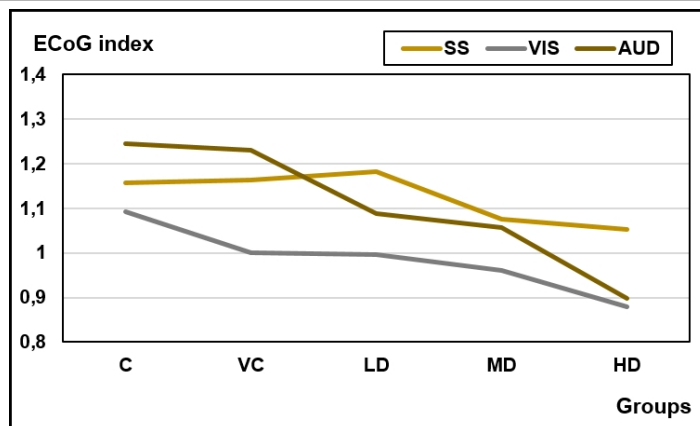
**Abbreviations:** GLM, general linear model; C, control; VT, vehicle treated; LD, low dose treated; MD, medium dose treated; HD, high dose treated.



**Supplementary Figure 4** Oxidative stress in the lungs of control and treated rats. **A**, TBARS reaction ( $\mu\text{M}$  malondialdehyde/mg protein); **B**, catalase activity (BU/mg protein).

**Notes:** Means+SD; n=10. \*, \*\*: p<0.05, 0.01 vs C; ##: p<0.01 vs VT.

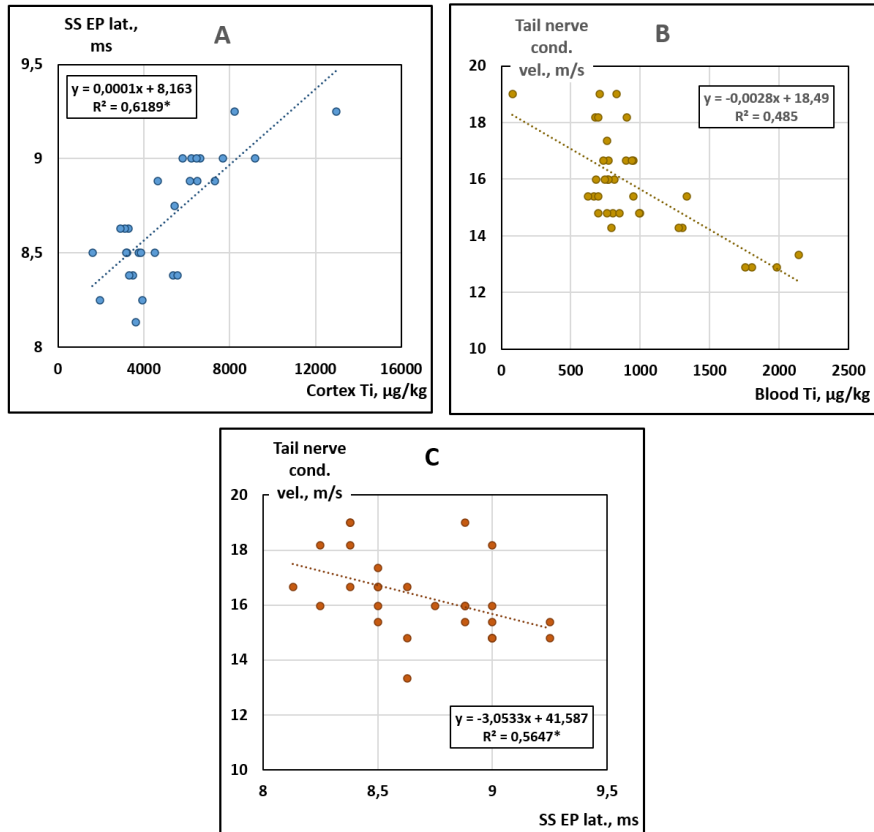
**Abbreviations:** BU, Bergmeyer units; TBARS, thiobarbituric acid reacting substances; C, control; VT, vehicle treated; LD, low dose treated; MD, medium dose treated; HD, high dose treated.



**Supplementary Figure 5** Alteration of the rats' spontaneous cortical activity in the three recorded areas, represented by the ECoG index, on effect of the nano-TiO<sub>2</sub> treatment.

**Notes:** Mean values, n=10. Error bars omitted for clarity.

**Abbreviations:** ECoG, electrocorticogram. *C*, control; *VT*, vehicle treated; *LD*, low dose treated; *MD*, medium dose treated; *HD*, high dose treated. *SS*, somatosensory area; *VIS*, visual area; *AUD* auditory area.



**Supplementary Figure 6** Linear correlations of the SS EP at 10 Hz and cortical Ti level (A), tail nerve conduction velocity and blood Ti level (B), and of the two electrophysiological parameters (C).

**Notes:** Straight line fitted by MS Excel, \*:  $p < 0.05$  (Fisher's F test).

**Abbreviations:** SS EP lat., somatosensory evoked potential latency; Tail nerve cond. vel., tail nerve conduction velocity.

