Supporting Information

Noble Metal Sensitized Invasive Porous Bioelectrodes: Advanced Medical Device for Enhanced Neuronal Activity and Chronic Alcohol Treatment

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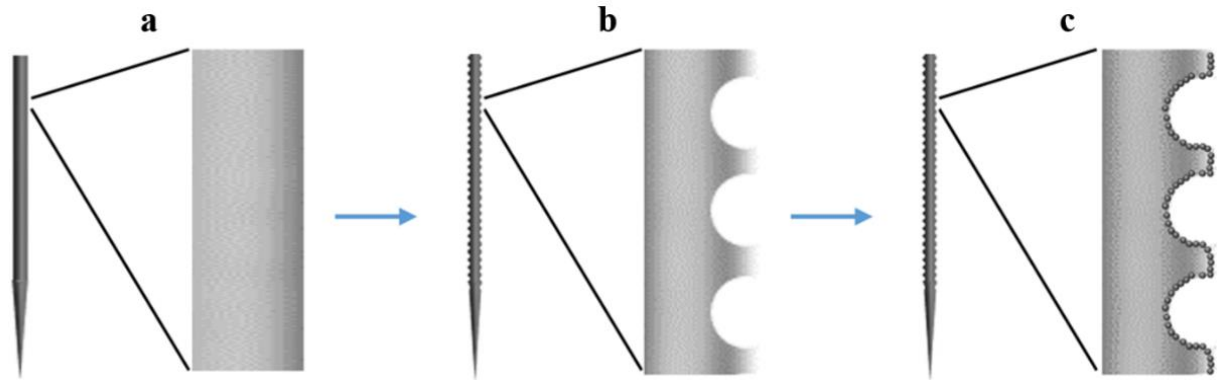

Fig. S1. Invasive bioelectrode surface modification strategy: (a) An invasive conventional bioelectrode (ICB), (b) An invasive porous bioelectrode (IPB) is formed by electrochemical anodization of ICB in a fluorine-based ethylene glycol electrolyte, and (c) Noble metal nanoparticles are electrodeposited on surface of IPB.

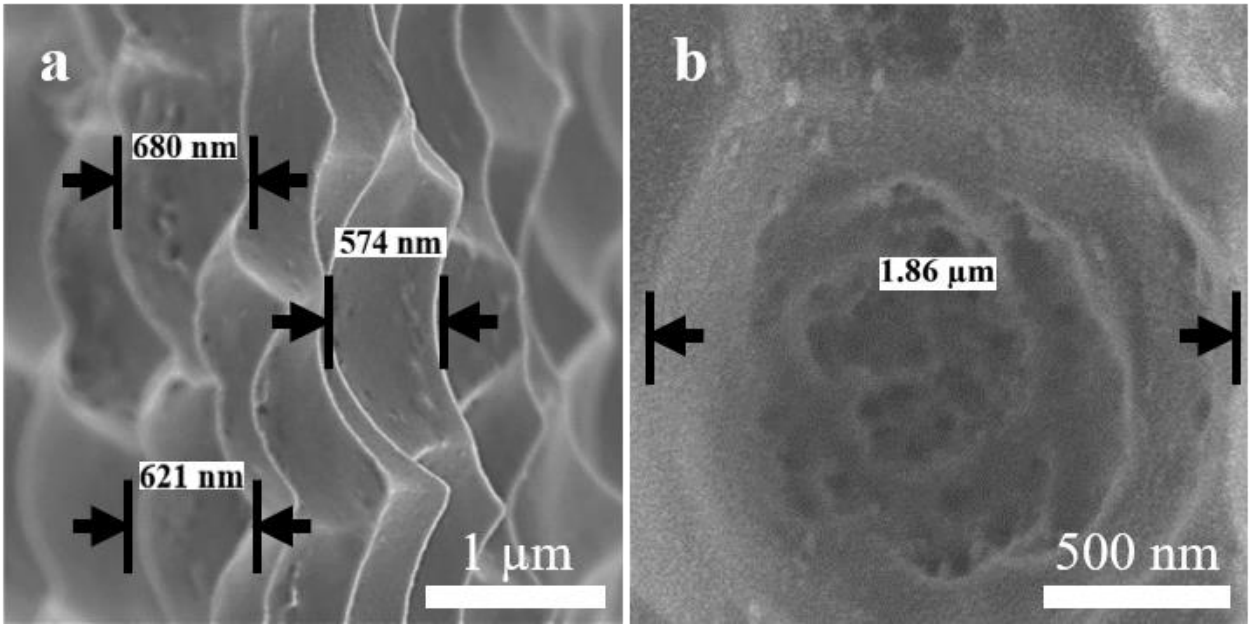

Fig. S2. High resolution FE-SEM images of invasive porous bioelectrode (IPB) showing: (a) cross-sectional image and (b) surface pore.

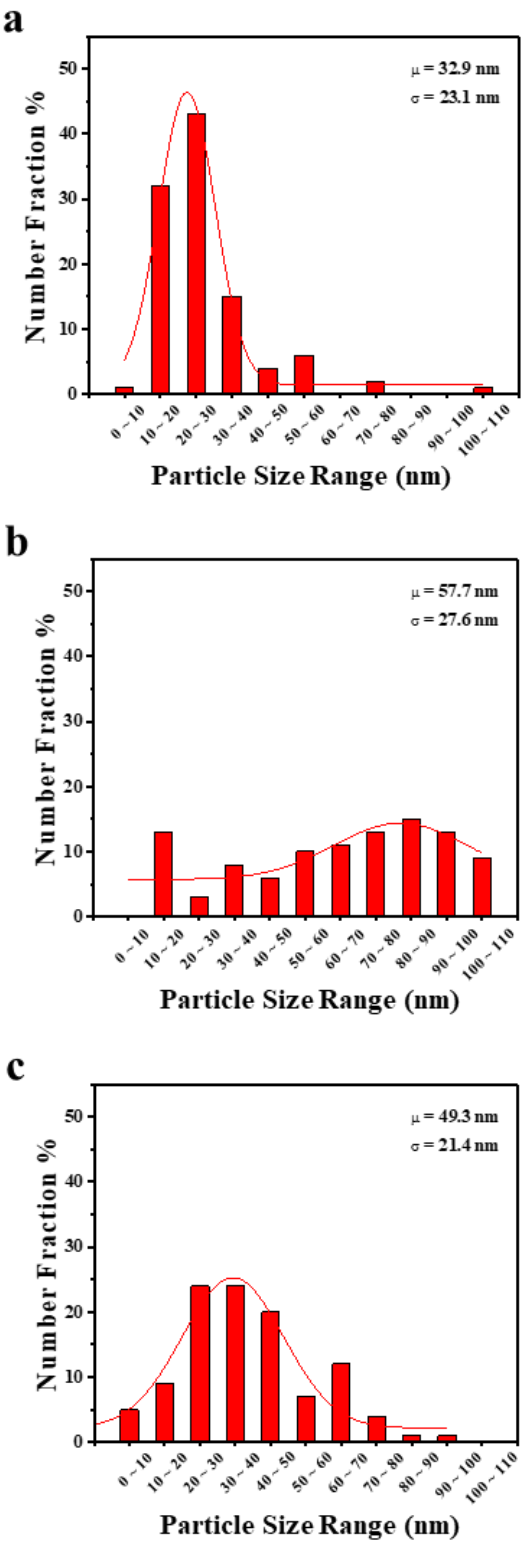

Fig. S3. Histograms showing size distribution of nanoparticles electrodeposited on invasive porous bioelectrode (IPB): (a) Ag, (b) Au and (c) Pt.

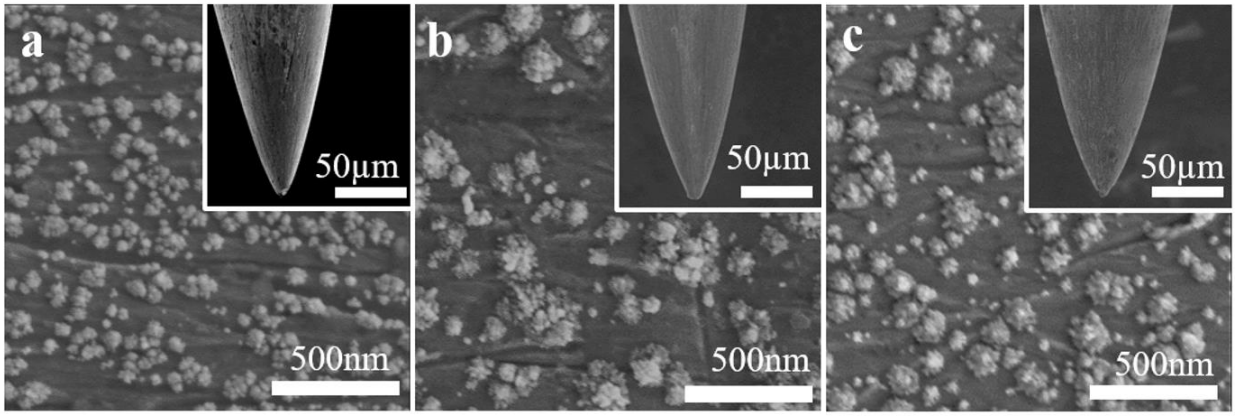

Fig. S4. FE-SEM surface images of nanoparticles electrodeposited onto invasive conventional bioelectrode (ICB): (a) Ag-ICB, (b) Au-ICB and (c) Pt-ICB. Inset shows tips of bioelectrodes.

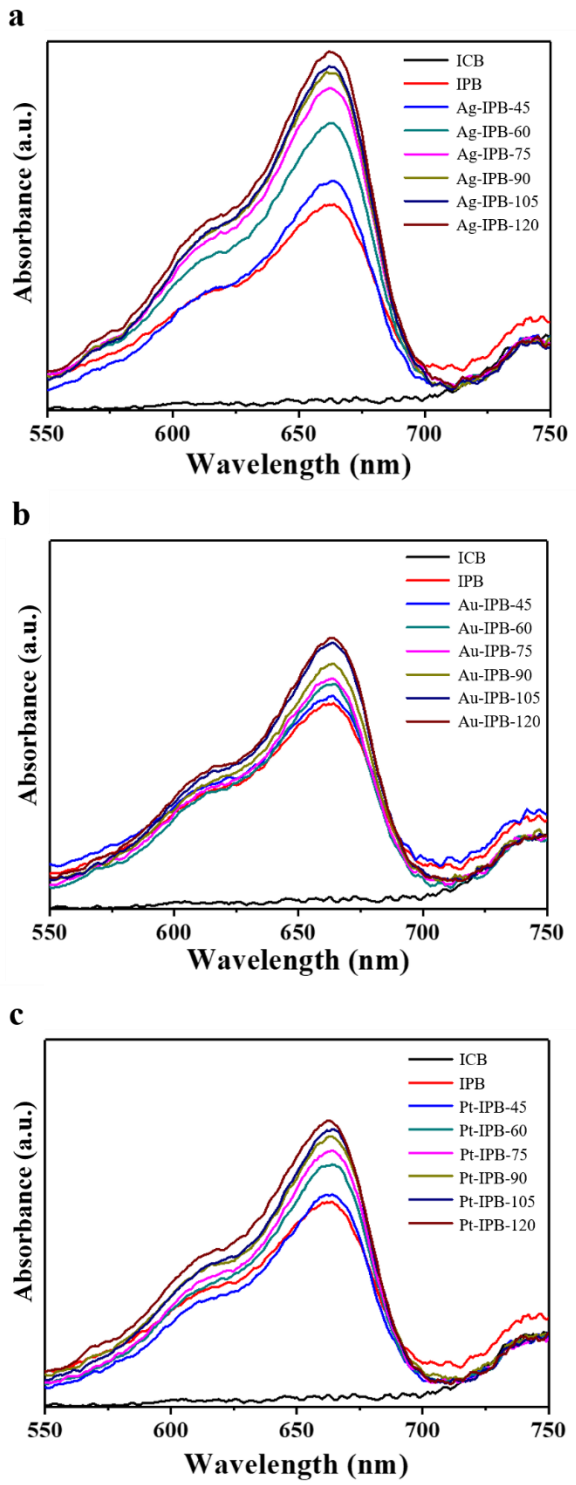

Fig. S5. Absorption spectra for methylene blue dye adsorbed on ICB, IPB, *x*-IPB with different electrodeposition times: (a) Ag-IPB, (b) Au-IPB and (c) Pt-IPB.

Sample	ICB	IPB	*x*-IPB-45	*x*-IPB-60	*x*-IPB-75	*x*-IPB-90	*x*-IPB-105	*x*-IPB-120
Deposition Conditions	-	-	2 V 45 s	2 V 60 s	2 V 75 s	2 V 90 s	2 V 105 s	2 V 120 s
Surface Area (m^2 g^{-1})	0.04	1.03	**Ag:** 1.17 **Au:** 1.06 **Pt:** 1.07	**Ag:** 1.40 **Au:** 1.16 **Pt:** 1.24	**Ag:** 1.49 **Au:** 1.18 **Pt:** 1.30	**Ag:** 1.55 **Au:** 1.29 **Pt:** 1.36	**Ag:** 1.57 **Au:** 1.36 **Pt:** 1.38	**Ag:** 1.64 **Au:** 1.38 **Pt:** 1.41

Table S1. Surface areas determined by methylene blue dye adsorption for ICB, IPB, and *x*-IPB (*x* = Ag, Au and Pt) with different electrodeposition times.

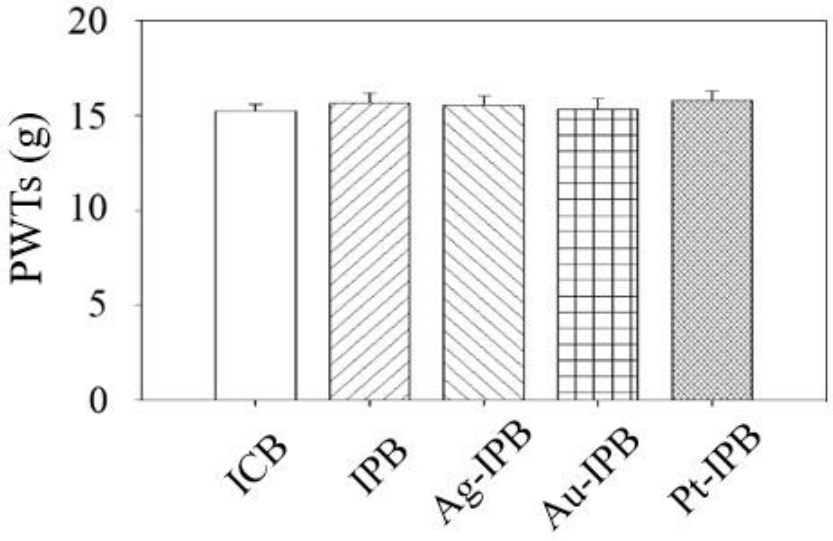

Fig. S6. Mechanical sensitivity in the paw withdrawal thresholds (PWTs) among ICB, IPB and *x*-IPB (where *x* = Ag, Au and Pt) groups before stimulation.

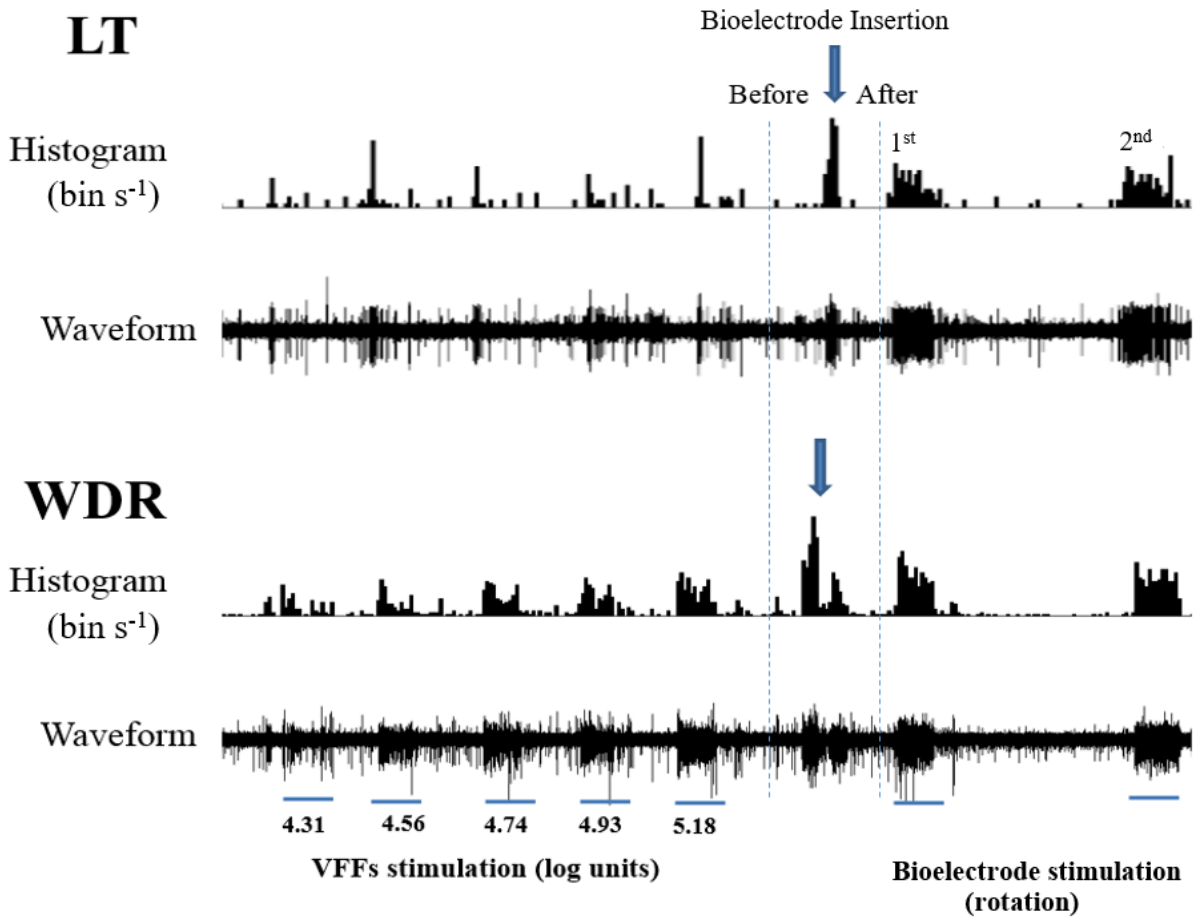

Fig. S7. Characterization of spinal dorsal horn neuronal phenotype and their response activity using invasive conventional bioelectrode.

Explanation: LT neurons (upper) showed strong response activity at only the initial mechanical stimulation, whereas WDR neurons (lower) showed strong activity during the VFFs stimulation. Arrow: the responses to bioelectrode insertion. Comparison of the response before and after bioelectrode insertion indicates no significant difference. Bar: Bioelectrode stimulation for 10 s; manual stimulation with rotation (rotation per second). 1^{st} and 2^{nd} indicate sequential 10 s bioelectrode stimulations.

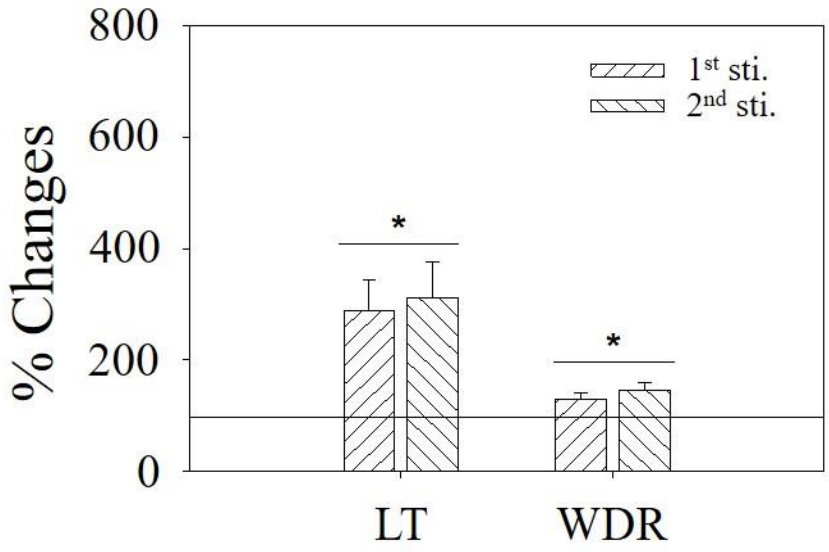

Fig. S8. Changes of neuronal responsiveness to stimulation for invasive conventional bioelectrode (ICB) groups.

Explanation: The activity of LT neurons (n = 26) with bioelectrode stimulation was 288.2 ± 56.5 % (1st bioelectrode stimulation) and 312.5 ± 63.9 % (2nd bioelectrode stimulation), showing a significant increase as compared to before stimulation (*$p < 0.05$). The activity of WDR neurons (n = 23) shows 129.1 ± 12.8 % (1st) and 146.6 ± 13.5 % (2nd). The comparison between 1st and 2nd stimulation does not show any significant changes. Horizontal line: 100 % of activity induced by VFFs stimulation.

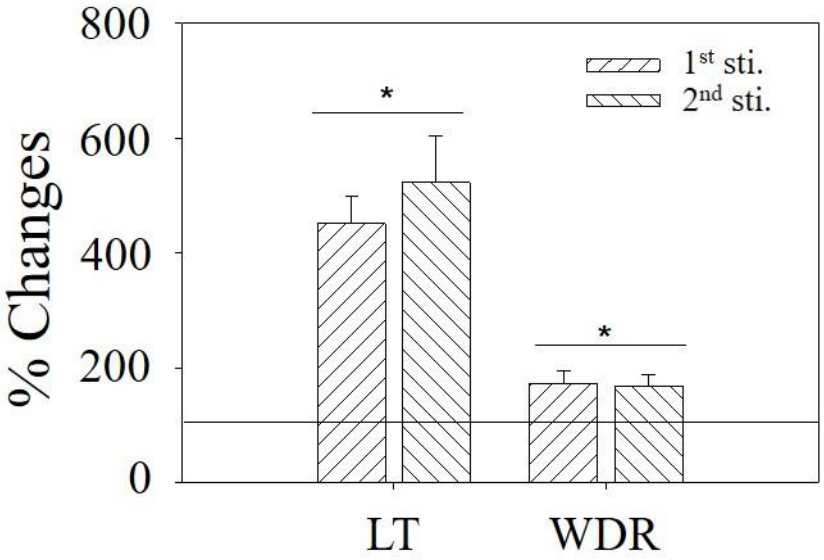

Fig. S9. Changes of neuronal responsiveness to stimulation for invasive porous bioelectrode (IPB) groups.

Explanation: The activity of LT neurons (n = 14) with bioelectrode stimulation was 451.8 ± 46.4 % (1st bioelectrode stimulation) and 522.8 ± 82 % (2nd bioelectrode stimulation), which shows a significant increase as compared to before stimulation (*$p < 0.05$). The activity of WDR neurons (n = 10) with bioelectrode stimulation was 173.6 ± 20.6 % (1st) and 168.1 ± 20.8 % (2nd) and also shows a significant increase (*$p < 0.05$). Comparison between 1st and 2nd stimulations shows little variation. Horizontal line: 100 % of activity induced by VFFs stimulation.

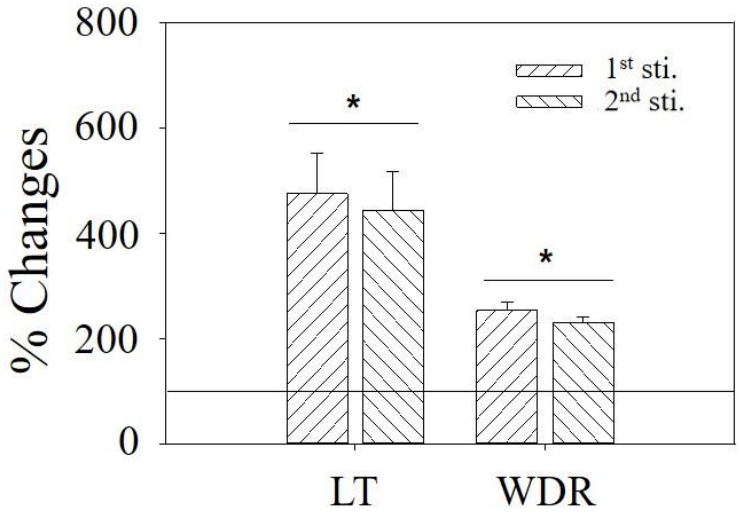

Fig. S10. Changes of neuronal responsiveness to stimulation in Ag-IPB groups.

Explanation: The activity of LT neurons (n = 14) with bioelectrode stimulation was 475.4 ± 77.5 % (1st bioelectrode stimulation) and 443.6 ± 74.2 % (2nd bioelectrode stimulation), thus showing a significant increase as compared to before stimulation (*$p < 0.05$). In addition, the activity of WDR neurons (n = 13) with bioelectrode stimulation was 253.6 ± 16.2 % (1st) and 230.7 ± 10.7 % (2nd), showing a significant increase (*$p < 0.05$). However, the comparison between the 1st and 2nd stimulations does not show a significant change. Horizontal line: 100 % of activity induced by VFFs stimulation.

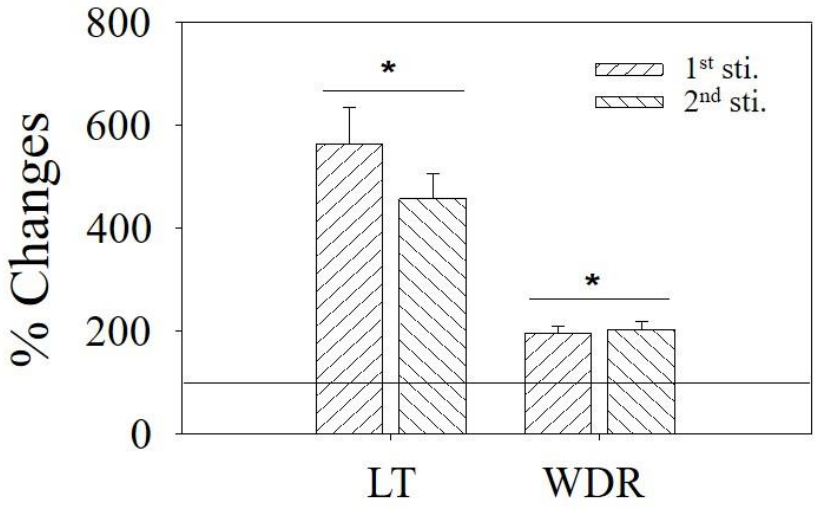

Fig. S11. Changes of neuronal responsiveness to stimulation in Au-IPB groups.

Explanation: The activity of LT neurons (n = 13) with bioelectrode stimulation is 562.9 ± 72.4 % (1^{st} bioelectrode stimulation) and 457.1 ± 49.5 % (2^{nd} bioelectrode stimulation), thus showing a significant increase as compared to before stimulation (*$p < 0.05$). In addition, the activity of WDR neurons (n = 15) with bioelectrode stimulation is 195.4 ± 13.2 % (1^{st}) and 203.1 ± 14.8 % (2^{nd}), thus displaying a significant increase (*$p < 0.05$). However, the comparison between 1^{st} and 2^{nd} does not show significant changes. Horizontal line: 100 % of activity induced by VFFs stimulation.

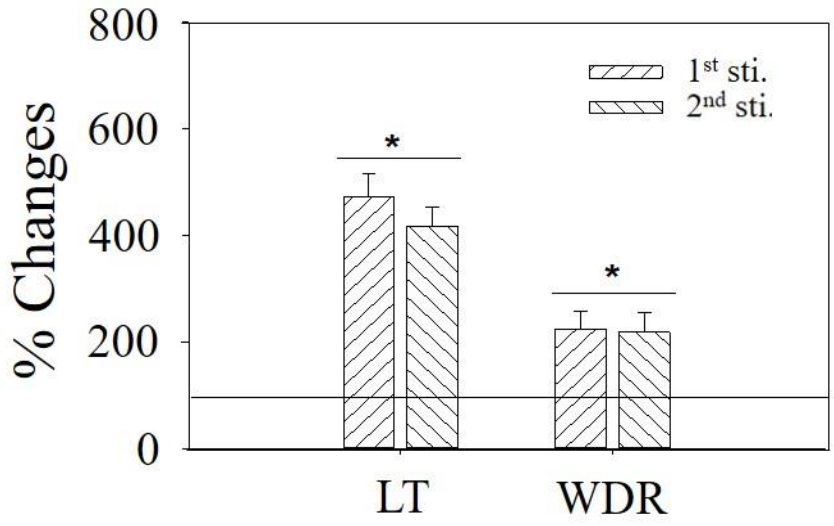

Fig. S12. Changes of neuronal responsiveness to stimulation in Pt-IPB groups.

Explanation: The activity of LT neurons (n = 14) with bioelectrode stimulation was 472.9 ± 42.7 % (1st bioelectrode stimulation) and 418.1 ± 36.35 % (2nd bioelectrode stimulation), showing a significant increase as compared to before stimulation (*$p < 0.05$). Moreover, the activity of WDR neurons (n = 12) with bioelectrode stimulation was 223.9 ± 33.8 % (1st) and 218.5 ± 36.1 % (2nd), which also exhibits a significant increase (*$p < 0.05$). However, the comparison between the 1st and 2nd stimulations does not show significant changes. Horizontal line: 100 % of activity induced by VFFs stimulation.