Acute acoustic trauma: contributions of inferior colliculus and ventrolateral orbital cortex

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Aims and objectives

Exposed to loud, prolonged sounds (acoustic trauma, AT) leads to the death of both inner and outer hair cells (IHCs and OHCs), death of neurons of the spiral ganglion and degeneration of the auditory nerve (1,2). Accumulating evidence suggests that acoustic trauma is linked to excessive neural activity in a distributed brain network that not only includes the central auditory pathway, but also extra-auditory brain regions (3). But exactly where and how noise affects the whole brain during acute period is unknown. To identify the neural substrate for these debilitating abnormalities, we induce bilateral severe hearing loss with broadband intense noise and use behavioral, electrophysiological, and functional magnetic resonance imaging (fMRI) techniques to identify the acute influence on rat brain.
Methods and materials

Subjects

Male SD rats weighing between 150-200 g were used. Animals were divided into two groups, each group has 12 rats. The noise group were exposed to intense broadband noise at 122 dB SPL for 2 hours, while the control subjects underwent sham exposure. All rats were conducted ABR test, Open Field test and rs-fMRI scan after noise exposure.

MRI acquisition and analysis

Each rat was positioned in the scanner in a prone position. Rectal temperature was maintained at 37.5°C with a temperature-controlled water blanket beneath the rat. The respiratory rate of the rat was monitored continuously during the entire experiment using an MRI-compatible pulse oximeter. Head position was stabilized with a bite bar and two rods located on opposite sides of the temporal surface of the head. MRI data were acquired with a 7.0 T animal MRI scanner (PharmaScan, Bruker Biospin GmbH, Germany) using a quadrature surface RF coil. Anatomical images were acquired with a turbo-rapid acquisition relaxation enhancement (RARE) T2-weighted sequence (repetition time (TR)/echo time (TE) = 3000/36 ms, slices = 22, field of view (FOV) = 3.2 × 3.2 cm, number of averages = 1, matrix = 256 × 256, slice thickness/gap = 1/0 mm, flip angle = 90°. The 22 contiguous anatomical images extended anteriorly from the cerebral-olfactory bulb to the caudal region of the cerebellum posteriorly. The BOLD measurements were acquired with a single-shot gradient-echo echo planar imaging (GE-EPI) sequence to acquire multiple slices of images. The parameters were: TR/TE = 2000/18 ms, slices = 21, FOV = 3.2 × 3.2 cm, number of averages = 1, matrix = 64 × 64, slice thickness/gap = 1/0 mm, flip angle = 90°, 100 volumes. Baseline and noise/control data acquisition occurred over a period of approximately 2 hr. Anatomical and functional scans were obtained from each rat before and 12 hr within noise exposure.

Data processing

The first 10 time points were eliminated to allow for scanner calibration and adaptation of the subject to the environment. Processing of the fMRI data was carried out with statistical Parametric Mapping software (SPM8, http://www.fil.ion.ucl.ac.uk/spm/). Sequential data processing steps included: slice-timing adjustment, realignment and correction for head-motion, spatial normalization to the standard rat brain atlas, detrending and filtering (0.01-0.1 Hz). Data were excluded if head movements exceeded 0.1 mm of maximum translation in the x, y, or z directions or 1.0 of maximum rotation about the three axes. Then we conducted ReHo analysis to evaluate rs brain activities.
Results

Bilateral acoustic trauma

As stated above in the method, both ears of the young adult rats were exposed to the broadband noise (122 dB SPL, 2h). ABR audiograms were obtained 2 weeks post noise and compared between the CN group and the (NE) group to determine differences in hearing sensitivity. Figure 1A revealed differences between the two groups, the frequency-averaged threshold was found to be 85.417 ± 6.463 dB SPL in the NE group, which was significantly higher than the value of 20.083± 8.853 dB SPL found for the control group (mean ± SD, n = 24; Student t test, t = 46.168, p < 0.001), showing that severe hearing loss was established in the noise group. And ABR threshold of the NE group were much higher than those of the CN group at every frequency tested (Figure 1B).

Behavioral test

NE rats tended to be less active than CN rats, displaying lower level of horizontal activity, total distance traveled (Figure 2C: T value=-2.289, DF=22, P=0.032) and mean velocity (Figure 2D: T value=-2.29, DF=22, P=0.032). Less number of rearing in NE group represented lower level vertical activity levels (Figure 2E: T value=-3.73, DF=22, P=0.001). We also assessed the anxiety level of rats by measuring the distance in the center area of open field apparatus. In this assessment, NE rats moved less distance in the center area of the apparatus than CN rats, however this difference was not statistically significant (Figure 2F: T value=-1.03, DF=22, P=0.312, maybe trend to perform less distance). From the open field test, it could be concluded that NE rats were more anxious than CN ones which therefore led us to concern about the anxiety symptoms of trauma noise exposure.

ReHo analysis

To identify the global effects of noise on brain activity, we compared the ReHo in the NE group with the CN group using two-sample t-tests corrected for multiple comparisons. Figure 3 reflects the regions where significant increases or decreases in ReHo were observed due to acoustic trauma; Table 1 shows the cluster sizes and t-values in left and right hemispheres for each region. Specifically, significant increases in ReHo occurred in left inferior colliculus (IC, 199 voxels, Figure 3A-C). In contrast, noise produced significant decreases in ReHo with left ventrolateral orbital cortex (VLO, 174 voxels, Figure 3D-E).

Correlation between behavioral test and ReHo value

Voxel-wise correlation analyses identified significant effects of the behavior variables on several brain regions in the both groups (Figure 4). Distance moved total was negatively correlated with the enhanced ReHo of IC in NE group. (Figure 4A, blue: r=-0.691;
P=0.013). However, ReHo value of CN group revealed no significant correlations with DMT (Figure 4A, black: r=-0.117; P=0.717). In addition, the weakened ReHo of VLO was not correlated with any of DMT (Figure 4B, CN group, black: r=0.218, P=0.029; NE group, blue: r=-0.296, P=0.351). Moreover, we found no positive correlations and none of the regions were correlated with other behavioral measures.
Fig. 1: Acoustic trauma induced ABR threshold shift. (A) Mean ABR thresholds before and after noise exposure. The differences between the two groups show that moderate-to-severe hearing loss was established in the noise group. (B) Mean ABR thresholds of different frequency 2 weeks post noise, including 2, 4, 8, 16, 32 kHz. Blue represents noise group, black represents control group. ***; P < 0.001.

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Fig. 2: Open field test of noise and control rats immediately post noise. Representative images show typical examples of control (A) and noise (B) rats exploring behavior in the open field test. Each group of rat was placed in the open field apparatus and their distance moved total (C), velocity mean (D), number of rearing (E) and distance in the center area (F) were measured. Blue represents noise group, black represents control group. *; P<0.05; ***; P<0.001. (n=12). Bars show the arithmetic mean and vertical lines represent the standard error of the mean.

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Fig. 3: Noise enhances and depresses regional homogeneity (ReHo) in specific CNS regions during the acute period. Panels A through E show MR images of rat brain. Significant differences in ReHo between the noise group vs control group 12h within post exposure. P<0.025 for voxel height and FWE corrected p<0.05 for cluster extent. IC, inferior colliculus; VLO, ventrolateral orbital cortex. Color heat map scale in lower right shows corrected t-values ranging from +4.16 to #4.91.

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<table>
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<tr>
<th>Brain region</th>
<th>Coordinate</th>
<th>Cluster size</th>
<th>Peak t-value</th>
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| ReHo increased
IC            | 27 24 -63 | 199          | 4.1579       |
| ReHo decreased
VLO           | 24 33 51  | 174          | -3.3222      |

**Table 1:** Acoustic trauma-induced changes in regional homogeneity (ReHo); Noise group vs Control group; Thresholds set at a corrected p value of <0.025 determined by FEW. Abbreviations: inferior colliculus (IC); ventrolateral orbital cortex (VLO).

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Fig. 4: Voxel-wise correlations between ReHo value and behavior parameters. Correlations in the noise group are represented by blue dots, while correlations in the control group are represented by black diamonds. Noise group: (A) distance moved total (DMT) was negatively correlated with ReHo value of inferior colliculus (R = -0.691, P = 0.013); (B) there is no correlation between DMT and ReHo value of VLO (R = -0.296, P = 0.351). No such correlations were observed in the control group (A-B, black lines and diamonds).

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Conclusion

To our knowledge, this present study is the first research to combine resting state functional MRI, electrophysiological measures and behavior test to identify changes across the whole brain induced by trauma noise exposure in the acute time. It investigated for the first time altered intraregional synchronization of several brain regions related to acoustic trauma by using resting-state ReHo and map out specific regions. Acoustic trauma depressed the auditory percept and induced anxiety-like behaviors immediately post exposure. Our results revealed significantly enhanced spontaneous neural activity in inferior colliculus and decreased activity in the ventrolateral orbital cortex which was involved in pain pathway. We demonstrate that acoustic trauma contributes to anxiety and pain; and inferior colliculus is not only the hub of auditory pathway, but also related to emotion.
Personal information

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References

