Altered Metabolism in the Developing Auditory Cortex of Chicks Exposed to Chronic High Decibel Noise: A proton NMR-based Metabonomic Study

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Introduction: This proton NMR-based metabonomic study examines the effect of high decibel sound exposure on the developing chick auditory cortex. Sound is one of the external stimuli which influence the development of the auditory system. However, with increasing industrialisation and modern social culture, exposure to high decibel sound (above 90 dB, often referred to as noise) is becoming inevitable and such high decibel chronic sound stimulation may disrupt the development of structures related to the auditory system and in turn may affect the proper development of hearing, storing and processing of complex sound and finally affecting cognition and behavior. However, the biochemical mechanisms responsible for chronic noise exposure induced changes are poorly understood, especially at the level of higher centers like auditory cortex. Here we have shown the effects of high decibel (110dB) chronic sound exposure, given in two forms- patterned (music) and un-patterned (noise), during prenatal development of chick (acoustic model-avian species). This study shows how the sound characteristics and pressure level affects the metabolic profile in the developing auditory cortex.

Methods: Fertilised eggs of White Leghorn chick (*Gallus gallus domesticus*) were exposed to chronic patterned (music) and unpatterned (noise) 110 dB sound during the incubation period (starting from E10 until hatching in 21day). On post hatch day 1, auditory cortex tissues were dissected out from control, music and noise exposed groups (n=10). Water soluble metabolites were extracted though homogenization in 6 % perchloric acid. Lyophilized samples were dissolved in deuterium oxide and trimethylsialylpropionate (TSP, used as internal reference and standard). Proton NMR Spectroscopy was carried out at 700 MHz (16.4 T, Agilent Technologies). One dimensional (1D) spectra and 2D spectra (zTOCSY) were acquired and the chemical shifts of resonances were referenced to TSP. Peaks of identified metabolites, including that of internal standard TSP, were integrated to obtain resonance signal intensity, which were used for the estimation of metabolite concentrations (mM/kg of wet weight of tissue). Data are expressed as mean ± SD and analyzed by one-way ANOVA and Student's t-test for comparison among three groups and two groups respectively.

Results: Figure 1 shows the proton NMR spectra obtained from the tissues of control, music and noise treated rats. Chronic noise exposure significantly decreases GABA level and increases the glutamate level (see Table 1). However, in music exposed groups, the decrease in GABA and increase in the glutamate did not show any significant difference as compared to control. A significant increase in glutamine level was observed in both groups as compared to control. Amount of α-Glucose, β-hydroxybutyrate and ATP were found to be significantly reduced in music and noise exposed groups. Levels of aspartate and N-acetyl aspartate showed significant decrease in the noise group only. Lactate levels tend to increase in both music and noise exposed groups. Creatine and taurine did not show any significant change in both groups except taurine in noise. Metabolites like choline, myo-inositol, alanine and valine were not affected by the high decibel exposure.

Metabolites	Control	Patterned (Music) 110dB	Un-patterned (Noise) 110dB
Glutamate	3.99 ± 0.5	4.51 ± 0.6	5.28 ± 0.8 *
GABA	1.88 ± 0.3	1.74 ± 0.2	1.59 ± 0.2 *
Glutamine	6.72 ± 0.7	8.28 ± 0.6 *	7.79 ± 0.6 *
Aspartate	1.07 ± 0.2	0.92 ± 0.1	0.84 ± 0.2 *
N-Acetylaspartate	2.72 ± 0.5	2.43 ± 0.5	2.02 ± 0.5 *
Taurine	7.61 ± 1.3	6.87 ± 1.0	6.22 ± 1.1 *
Creatine	4.82 ± 0.8	4.33 ± 0.6	4.21 ± 0.7
Choline	1.29 ± 0.1	1.33 ± 0.5	1.50 ± 0.3
Myo-Inositol	6.85 ± 1.6	7.57 ± 1.0	7.79 ± 1.7
α-Glucose	0.94 ± 0.1	0.74 ± 0.04 *	0.67 ± 0.06 *
Lactate	4.98 ± 0.9	5.83 ± 0.9	6.06 ± 1.2
ATP	1.12 ± 0.1	0.94 ± 0.06 *	0.86 ± 0.1 *
β-Hydroxybutyrate	0.67 ± 0.1	0.49 ± 0.1 *	0.39 ± 0.1 *
Alanine	0.85 ± 0.1	0.93 ± 0.2	0.77 ± 0.2
Valine	0.16 ± 0.05	0.14 ± 0.04	0.12 ± 0.03

Table: 1 (* p<0.5: significant difference from control)

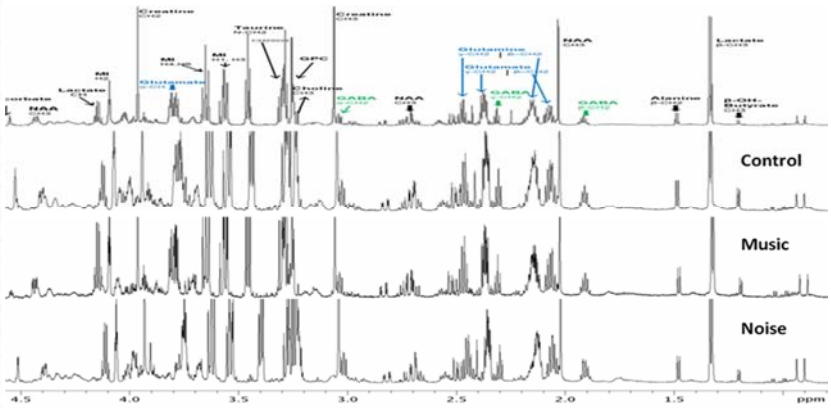

Fig: 1

Discussion: Increase in the glutamate level with chronic noise exposure could lead to excitotoxicity, while decrease in GABA level could alter the excitatory and inhibitory balance, overall resulting into an enhanced excitatory response. However, in music exposed groups, the decrease in GABA and increase in glutamate did not show any significant difference despite high decibels. Such a differential effect between noise and music exposure proves that sound characteristics has profound effect on the activity of auditory cortex. Creatine and taurine (known positive allosteric modulators of GABAergic system) levels remain unchanged in both groups except taurine in noise, representing a compensatory approach against the increased excitatory response. Decrease in the amount of metabolites involved in energy metabolism indicates an increased neuronal activity at 110 dB sound exposure. Lactate levels tend to increase in both music and noise exposed groups suggesting an increased glial contribution towards the enhanced neuronal energy demand. In summary, high decibel un-patterned noise stimulation can alter the excitatory and inhibitory balance through increased glutamate and decreased GABA levels. Patterned sound stimulation however prevented any negative changes despite high decibel levels. High sound pressure levels independent of sound characteristics, led to increased energy demand resulting in the altered energy metabolism. Thus, high decibel sound can significantly disturb the metabolism of the auditory cortex and in turn its development and maturation

References: (1) Wei Suna, et al., Neuroscience. 2008; 156: 374–380; (2) Li I. et al., PNAS, 2002; 99, 2309–2314; (3) Koga Y, et al., Neuroscience, 2005; 132: 65-71.