Study of the inferior colliculus in patients with schizophrenia by magnetic resonance spectroscopy

Beatriz Martínez-Granados, M. Carmen Martínez-Bisbal, Julio Sanjuán, Eduardo J. Aguilar, Luis Martí-Bonmatí, Enrique Mollá, Bernardo Celda

Introduction. Previous studies have suggested morphometric and functional abnormalities in the inferior colliculus in patients with schizophrenia. Auditory hallucinations are one of the central symptoms in schizophrenia. In this complex and multidimensional event both attention and emotion are thought to play a key role.

Aim. To study metabolic changes in the inferior colliculus, a nucleus integrated in the auditory pathway, in patients with schizophrenia and the possible relationship with auditory hallucinations.

Subjects and methods. Magnetic resonance spectroscopic imaging studies were performed in 30 right-handed patients with chronic schizophrenia (19 of them with auditory hallucinations) and 28 controls. A magnetic resonance spectroscopic imaging 2D slice was acquired and the voxels representative of both inferior colliculi were selected. N-acetylaspartate (NAA), creatine (Cr) and choline (Cho) peak areas were measured.

Results. The patients with schizophrenia showed a NAA/Cr significant reduction in the right inferior colliculus compared to the control subjects. The metabolic data in the right inferior colliculus were correlated with emotional auditory hallucinations items.

Conclusions. The contribution of the inferior colliculus on neural underpinnings of auditory hallucinations is particularly relevant for the right inferior colliculus and is centered on attention-emotional component of this symptom.

Key words. Attention. Auditory hallucinations. Inferior colliculus. Magnetic resonance spectroscopy. N-acetylaspartate. Schizophrenia.

Department of Physical Chemistry; University of Valencia (B. Martínez-Granados, M.C. Martínez-Bisbal, B. Celda). CIBER Bioengineering, Biomaterials and Nanomedicine, CIBER-BBN (B. Martínez-Granados, M.C. Martínez-Bisbal, B. Celda). CIBER Mental Health Network, CIBERSAM (J. Sanjuán, E.J. Aguilar). Department of Psychiatry; University of Valencia; Fundación Hospital Clínico (J. Sanjuán, E.J. Aguilar). Radiology Department; La Fe University and Polytechnic Hospital; Valencia (L. Martí-Bonmatí). Radiology Department; La Ribera Hospital; Alzira, Valencia (E. Mollá).

Corresponding author:
Dr. Bernardo Celda Muñoz. Department of Physical Chemistry. University of Valencia. Doctor Moliner, 50. E-46100 Burjassot (Valencia).

Fax:
+34 963 543 213.

E-mail:
bernardo.celda@uv.es

Funding:
Spanish national grant SAF2007-65473, European Integrated Projects eTUMOUR (FP6-2002-LIFESCIHEALTH 503094) and CENIT MIND.

Acknowledgments:
Asociación para el Desarrollo y la Investigación en Resonancia Magnética (ADIRM).

Accepted:
13.02.14.

How to cite this paper:
Martínez-Granados B, Martínez-Bisbal MC, Sanjuán J, Aguilar EJ, Martí-Bonmatí L, Mollá E, et al. Study of thew inferior colliculus in patients with schizophrenia by magnetic resonance spectroscopy. Rev Neurol 2014; 59: 1-7.

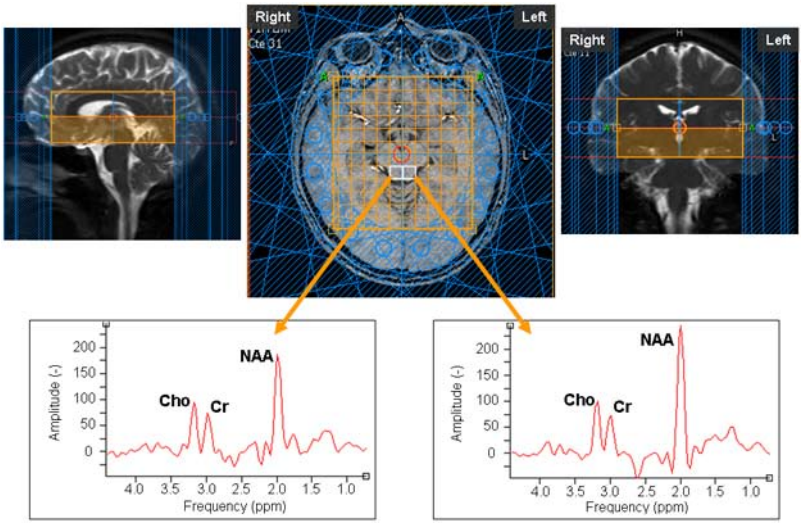
Versión española disponible en www.neurologia.com

Introduction

The causes of auditory hallucinations in psychotic patients are not yet completely understood. In fact, auditory verbal hallucinations are known to be multidimensional and probably have different neural underpinnings that can help to explain such a complex event beyond a single deficit theory [1].

Currently, auditory hallucinations are considered as a failure of attribution of emitter source, so those patients perceive as external their own inner speech. Auditory hallucinations may be related to the pathways in which real auditory stimuli are involved. The inferior colliculus is a nucleus integrated in the auditory pathway that modulates the auditory stimulus and, with other nuclei, contributes to the spatial location of sound [2]. Interestingly, functional magnetic resonance imaging (fMRI) has revealed the activation of the right inferior colliculus, among other brain structures, with auditory hallucinations in patients with schizophrenia [3]. Moreover, a recent study in 28 patients with schizophrenia found a reduction in the volume of the right inferior colliculus, compared with the control subjects [4], suggesting that a structural abnormality of the inferior colliculus may be involved in the auditory cognitive dysfunction in these patients. However, there is no previous spectroscopy study of the inferior colliculus in schizophrenia. Proton magnetic resonance spectroscopy (^{1}H MRS) allows non-invasive in vivo study of neurometabolic profile [5]. N-acetylaspartate (NAA), creatine (Cr) and choline (Cho) are the metabolites most frequently studied by ^{1}H MRS in the central nervous system diseases. NAA is mainly located in neurons and is a marker of their viability and function [5]. Likewise, NAA plays a role in mitochondrial oxidative metabolism [6]. Cr is a marker for cell density and is involved in the cellular energy metabolism. The Cr peak at 1.5 T refers to the sum of Cr and phosphocreatine [5]. Cho, as a precursor for the neurotransmitter acetylcholine and membrane compounds (such as phospholipids including phosphatidylcholine, glycerophosphocholine and sphingomyelin), is

Figure. Sagittal, axial and coronal anatomical images showing the orientation of MRSI slice and the spectra of the voxels that include the inferior colliculus in both hemispheres.



related with the turnover of membranes [5-7]. ^{1}H MRS has shown metabolic changes in several brain regions like the temporal lobes, the frontal cortex and the thalamus in patients with schizophrenia [8]. Moreover, it has already been demonstrated that thalamic spectroscopic metabolic abnormalities correlates to auditory hallucinations in patients with schizophrenia [9].

The aim of this work is to study the biochemical changes in the inferior colliculus, which is involved in the auditory pathway, in right-handed male patients with chronic schizophrenia, both suffering and not suffering from auditory hallucinations, and in healthy group. Possible associations with psychotic symptoms and auditory hallucinations (globally and dimensionally assessed) will also be investigated.

Subjects and methods

Sample

The study included 30 male right-handed patients who met DSM-IV [10] criteria for schizophrenia. The mean age was 42 ± 11 years (± S.D.). The mean educational level of patients with schizophrenia in a numeric system was 3.9 (range 1 as illiterate to 5 as university level). The mean duration of illness was 15.2 ± 10.0 years. All of them were under antipsychotic treatment at the time of evaluation: 2 with a first-generation antipsychotic, 19 with second-generation antipsychotic and 9 with a combined treatment (first- and second-generation antipsychotic). The patients with schizophrenia were divided according with the presence of auditory hallucinations: 19 were patients with chronic schizophrenia and chronic auditory hallucinations (40 ± 8 years) and 11 were patients with chronic schizophrenia but without auditory hallucinations (44 ± 15 years) and they have never had them. The diagnosis was confirmed by clinical consensus between 2 psychiatrists.

The control group comprised 28 healthy male right-handed volunteers. Their mean age was 33 ± 11 years and their mean educational level was 5. Control subjects with a psychiatric history or presence of perceptual abnormalities were previously excluded.

It can be stated that there were no auditory problems in any of the subject, both patients and controls. All participants gave written informed consent for the study participation after being fully informed of the procedures. The study was approved by the local ethical committee.

Psychopathological assessments

All the patients were clinically assessed for the presence and dimensions of auditory hallucinations by the Spanish version of the Psychotic Symptom Rating Scale (PSYRATS) [11], a specific scale to measure auditory hallucinations. This scale assesses 11 different parameters about auditory hallucinations: frequency, duration, location, loudness, belief reorigin, amount of negative content, degree of negative content, amount of distress, intensity of distress, disruption and grade of control. They were also clinically assessed with the 24-item Brief Psychiatric Rating Scale (BPRS) [12], in order to control for the presence of general psychopathology in this sample of psychotic patients.

The mean score was 30.2 (range 22-39, SD 5.1) and 44.0 (range 24-67, SD 11.2) for PSYRATS and BPRS, respectively.

Procedures

Magnetic resonance imaging and spectroscopic imaging (MRI/MRSI) studies were performed at 1.5 T system (Gyroscan Intera, Philips Medical Systems, The Netherlands) using a standard head coil. Participants were placed in the supine position and

Table I. Mean ± SD of the inferior colliculus metabolite ratios in each type of subjects and statistical significance of different comparison: patients with schizophrenia vs. controls; and patients with auditory hallucinators vs. patients without auditory hallucinators vs. controls.

	Right inferior colliculus				Left inferior colliculus			
	Schizophrenics		Controls	ANOVA	Schizophrenics		Controls	ANOVA
	AH	N-AH			AH	N-AH		
NAA/Cr	2.58 ± 0.68		3.15 ± 0.69	$p = 0.003$ [a]	2.93 ± 0.74		3.16 ± 0.51	$p = 0.056$ [a]
	2.59 ± 0.69	2.58 ± 0.70		$p = 0.013$	3.05 ± 0.83	2.72 ± 0.52		$p = 0.091$
Cho/Cr	1.19 ± 0.19		1.29 ± 0.23	$p = 0.091$ [a]	1.18 ± 0.16		1.23 ± 0.20	$p = 0.255$ [a]
	1.20 ± 0.20	1.18 ± 0.19		$p = 0.232$	1.19 ± 0.17	1.16 ± 0.13		$p = 0.489$
NAA/Cho	2.23 ± 0.63		2.40 ± 0.47	$p = 0.099$ [a]	2.52 ± 0.66		2.61 ± 0.51	$p = 0.276$ [a]
	2.32 ± 0.71	2.06 ± 0.39		$p = 0.110$	2.60 ± 0.72	2.37 ± 0.53		$p = 0.382$

AH: auditory hallucinators; Cho: choline; Cr: creatine; NAA: N-acetylaspartate; N-AH: no auditory hallucinators. [a] *t* test.

their head was secured with foam padding. In all subjects, both a three plane T2-weighted turbo spin echo image localizer and an axial whole brain T1-weighted spoiled gradient echo (sFFE) image (TR = 7 ms, TE = 1.91 ms, field of view (FOV) = 220 mm, slice thickness = 1.25 mm), oriented parallel to the line through the anterior and posterior commissures, were performed. Multislice ^{1}H MRSI with a two dimensional turbo spectroscopic imaging sequence (2DTSI) was performed using an orientation and a FOV identical to the T1 weighted images, with two slices of 23 mm section thickness (Figure). Point resolved echo spectroscopy sequences (PRESS) were used with the followed acquisition parameters: TR = 2700 ms, TE = 272 ms, data points = 256, zero-filled to 512 prior to Fourier transform, time acquisition = 9.29 min, spectral width = 1050 Hz, matrix of 24 × 24 elements and a region of interest 110 × 100 × 23 mm with a voxel size of 1.93 cm^3.

In the analysis of MRSI, one element of volume (9.17 × 9.17 ×23 mm, 1.93 cm^3) representative of each inferior colliculus from right and left hemisphere was chosen, with the help of a radiologist, in the lower slice (Figure). Both, right and left spectra of inferior colliculus were evaluated separately. The areas of NAA, Cr and Cho resonances were integrated with jMRUI program [13,14]. NAA and Cho metabolites were expressed as Cr ratios. The NAA/Cho ratio was also evaluated.

Statistical analysis

The normal distributions of measurements were tested using the Shapiro-Wilks test. Metabolic analysis between patients with schizophrenia and control group was performed using *t*-tests. On the other hand, analysis of variance (ANOVA) with multiple comparisons was used to analyze the differences between patients with schizophrenia and auditory hallucinations, patients with schizophrenia without auditory hallucinations and control group. The post hoc test used for checking the statistical differences between each two individual groups was a Bonferroni test. Pearson and Spearman rank correlation coefficients were used for correlation analysis. Finally, analysis of age as a covariant was done for checking the influence among different variables. The criterion of significance was set at $p < 0.05$. SPSS 14.0 program was used for statistical analysis.

Results

In the comparison between patients with schizophrenia and control subjects both inferior colliculi showed a reduction of NAA/Cr ratio in patients with schizophrenia. This reduction was only statistical significance in the right inferior colliculus (Table I).

Table II. Correlations between the clinical data and the inferior colliculus metabolic ratios.

		Right inferior colliculus			Left inferior colliculus		
		NAA/Cr	Cho/Cr	NAA/Cho	NAA/Cr	Cho/Cr	NAA/Cho
BPRS [a]	Schizophrenics	-0.12 (0.543)	+0.11 (0.582)	-0.01 (0.950)	-0.16 (0.414)	+0.09 (0.651)	-0.19 (0.311)
	AH	-0.15 (0.549)	+0.24 (0.319)	-0.28 (0.254)	-0.33 (0.163)	+0.16 (0.508)	-0.41 (0.078)
	N-AH	-0.14 (0.679)	-0.19 (0.567)	+0.24 (0.510)	-0.12 (0.729)	-0.18 (0.601)	+0.01 (0.999)
Age of onset of auditory hallucinations [b]		-0.26 (0.290)	-0.23 (0.342)	-0.24 (0.316)	-0.08 (0.731)	-0.07 (0.767)	+0.07 (0.781)
Chlorpromazine equivalents doses [b]	Schizophrenics	-0.18 (0.360)	-0.25 (0.206)	+0.10 (0.617)	-0.20 (0.320)	-0.22 (0.260)	-0.73 (0.711)
	AH	-0.20 (0.467)	-0.20 (0.442)	-0.03 (0.901)	-0.34 (0.180)	-0.28 (0.280)	-0.19 (0.471)
	N-AH	-0.31 (0.358)	-0.56 (0.076)	+0.26 (0.467)	-0.25 (0.454)	-0.18 (0.603)	-0.14 (0.681)
Age [b]	Schizophrenics	-0.13 (0.518)	+0.21 (0.270)	-0.26 (0.169)	-0.14 (0.475)	+0.28 (0.130)	-0.28 (0.130)
	Controls	-0.02 (0.917)	+0.26 (0.189)	-0.19 (0.354)	-0.03 (0.897)	+0.11 (0.571)	-0.09 (0.640)

AH: auditory hallucinators; Cho: choline; Cr: creatine; NAA: N-acetylaspartate; N-AH: no auditory hallucinators. [a] The Spearman's rank correlation coefficients (rho) and significance (*p* value); [b] Pearson's correlation coefficients (*r*) and significance (*p* value).

In the comparison between patients with schizophrenia and auditory hallucinations, patients with schizophrenia without auditory hallucinations and control subjects, ANOVA analysis showed statistical significant differences in NAA/Cr ratio in the right inferior colliculus (Table I). Post-hoc Bonferroni analysis showed statistical significance between patients with schizophrenia and auditory hallucinations and control subjects (p=0.030). The comparison of patients with and without auditory hallucinations did not show statistical significant differences in this location.

Finally, covariance analysis to evaluate the individual influence of age in MRS ratios did not show any statistical significance.

In the comparison between metabolic and clinical data, there were no statistical significant correlations between the metabolic data and the general psychotic symptoms severity (BPRS), duration of illness, age of onset of auditory hallucinations, Chlorpromazine equivalents doses, age of subjects (Table II) and psychopathological variable globally assessed auditory hallucinations (PSYRATS) (Table III). However, for patients with auditory hallucinations several dimensions of auditory hallucinations were correlated significantly with the metabolic data. In particular, amount of negative content (right inferior colliculus: NAA/Cr, NAA/Cho; left inferior colliculus: NAA/Cr), degree of negative content (right inferior colliculus: NAA/Cr; left inferior colliculus: Cho/Cr), amount of distress (right inferior colliculus: NAA/Cr) and intensity of distress (right inferior colliculus: NAA/Cr, NAA/Cho) were correlated. These data are showed in Table III.

Discussion

The main findings of this study show metabolic differences between the control subjects and the patients with schizophrenia and auditory hallucinations in the right inferior colliculus and an association between the metabolic data in the right inferior colliculus and the emotional component of auditory hallucinations.

The lower NAA/Cr ratio observed in patients with schizophrenia and auditory hallucinations can be mainly related to a decrease in NAA amount in the right inferior colliculus. This is because the Cr signal intensity (3.02 ppm) is thought to be relatively constant between individuals and in most brain areas [5], with some exceptions such as some brain lesions [15]. As it was suggested for the thalamus [9], a NAA decrease might indicate reduction in the

Table III. Correlations between dimensions of auditory hallucinations and the inferior colliculus metabolic ratios in patients with auditory hallucinations [a].

	Right inferior colliculus			Left inferior colliculus		
	NAA/Cr	Cho/Cr	NAA/Cho	NAA/Cr	Cho/Cr	NAA/Cho
PSYRATS	-0.39 (0.241)	-0.38 (0.224)	-0.43 (0.169)	-0.41 (0.185)	-0.15 (0.632)	-0.27 (0.389)
Frequency	+0.40 (0.229)	-0.02 (0.963)	+0.29 (0.366)	+0.30 (0.347)	+0.39 (0.209)	-0.13 (0.686)
Duration	+0.40 (0.227)	+0.10 (0.767)	+0.32 (0.316)	+0.41 (0.192)	+0.24 (0.461)	+0.18 (0.583)
Location	+0.29 (0.389)	-0.20 (0.535)	+0.07 (0.823)	+0.00 (1.000)	-0.01 (0.982)	+0.05 (0.867)
Loudness	+0.37 (0.261)	-0.06 (0.850)	+0.43 (0.166)	+0.09 (0.777)	-0.28 (0.387)	+0.37 (0.241)
Beliefs about origin of voices	+0.06 (0.864)	+0.20 (0.536)	-0.45 (0.143)	-0.24 (0.447)	+0.36 (0.249)	-0.57 (0.055)
Amount of negative content	-0.83 (0.002)	-0.38 (0.221)	-0.79 (0.002)	-0.73 (0.007)	-0.24 (0.444)	-0.48 (0.113)
Degree of negative content	-0.74 (0.009)	-0.41 (0.186)	-0.17 (0.596)	-0.27 (0.390)	-0.58 (0.048)	+0.19 (0.547)
Amount of distress	-0.66 (0.028)	+0.03 (0.927)	-0.34 (0.273)	-0.23 (0.473)	-0.01 (0.973)	-0.17 (0.589)
Intensity of distress	-0.66 (0.028)	-0.26 (0.416)	-0.65 (0.021)	-0.47 (0.125)	-0.12 (0.717)	-0.38 (0.218)
Disruption to life	-0.27 (0.420)	-0.21 (0.510)	-0.39 (0.207)	-0.26 (0.421)	-0.11 (0.735)	-0.14 (0.657)
Controllability of voices	-0.20 (0.547)	-0.39 (0.212)	-0.27 (0.395)	-0.57 (0.054)	-0.50 (0.099)	+0.01 (0.972)

Cho: choline; Cr: creatine; NAA: N-acetylaspartate. [a] Data are the Spearman's rank correlation coefficients (rho) and significance (*p* value).

number of neurons or neuronal dysfunction of the right inferior colliculus.

Likewise, it has been reported that impairment of certain cognitive functions mediated by the dorsolateral prefrontal cortex observed in patients with schizophrenia may be related to changes in the excitatory neurotransmission of glutamate (Glu) [16]. In patients with tinnitus, a hearing disorder, the increased activity of the colliculus would be perceived in the auditory cortex as auditory hallucinations [17]. This would be in concordance with the data reported by fMRI that shows an increased activity of the right inferior colliculus in patients with auditory hallucinations [3]. An excess in Glu may cause neuronal damage by excitotoxicity associated with excessive intracellular calcium [18]. In the present study the resonances of Glu are not observed because of the long TE used (272 ms). Nevertheless, the neuronal damage would be reflected by the decrease observed in NAA, a marker of neuronal viability, in the right inferior colliculus of patients with schizophrenia and auditory hallucinations.

The NAA decrease observed in this study in the right inferior colliculus could be related to the decrease in transmission of the auditory stimulus through the right ear, also linked with the impairment in the left hemisphere language areas described in patients with schizophrenia (mainly in those with auditory hallucinations) through studies using dichotic listening test [19]. Furthermore, the involvement of the inferior colliculus may not only be related to the attention impairment but also with an alteration in the perception of sounds. It has been reported that a weak acoustic pre-stimulus prior to acoustic stimulation reduces the perception of that sound. The inhibition of the perception of sound has been found to be poor in patients with schizophrenia [20]. Moreover, these sensorimotor deficits have been linked to alterations at the level of the inferior colliculus, so this structure may play a role in the perception of sounds [21]. These results suggest that central inhibitory mechanisms may be damaged in patients with schizophrenia [20] according to investigations describing pre-

dominance of excitatory activity of the right inferior colliculus.

The correlations between the NAA/Cr ratio in the right inferior colliculus and the items 'amount of negative content', 'degree of negative content', 'amount of distress' and 'intensity of distress' (Table III) constitute a striking finding that can help to understand some characteristics of auditory hallucinations in psychotic patients. In a previous study about aggressiveness in patients with schizophrenia and chronic auditory hallucinations, a positive correlation between functional activation associated with verbal emotional stimulus in the left hippocampus and the right middle frontal gyrus with the degree of aggressiveness was observed [22]. On the other hand, the inferior colliculus is a central structure in processing the behavioral and emotional significance of acoustic stimuli. Together with other structures such as the hypothalamus, the amygdala, the dorsal periaqueductal gray and the superior colliculus, the inferior colliculus constitute the neural substrates of the defense system through the integration of aversive states in the brain and the production of defense responses such as fear and stress response [23]. It seems therefore that abnormalities in the right inferior colliculus are associated with a more distressing perception of auditory hallucinations. Compared with the amygdala, the inferior colliculus has not received great attention as part of these defense neural systems in humans. We hypothesize that while other upper structures may give the auditory hallucinations the qualities of loudness, outer origin, personal meaning or lexical complexity, the abnormalities in the inferior colliculus (and may be in other structures in the auditory pathway) can be responsible for the distress provoked by this event which could finally be understood as an alteration in the auditory mediated defense mechanism. Our findings are also in support of recent suggestion by Hoffman of the role of listening attitude to voices [24].

The potential effect of antipsychotic treatment in inferior colliculus metabolism and the age differences between patients with schizophrenia and control subjects could be a limitation of this study. However, we haven't found any correlations neither between metabolic data and Chlorpromazine equivalent doses nor between metabolic data and age (Table II). Moreover, the age as a covariant did not show any statistical significant effect in the metabolites ratios. On the other hand, the small metabolic differences in inferior colliculus between patients with schizophrenia with and without auditory hallucinations should be confirmed with the study of a larger population. Spectroscopy studies with short TE are also needed to confirm the alterations of Glu in inferior colliculus.

In conclusion, this study shows metabolic changes indicative of neuronal damage in the right inferior colliculus of patients with schizophrenia compared with control group. The metabolic alteration in the inferior colliculus might not only reflect attention deficits but might also reflect a disorder in the filter of perception of the sound source. The neuronal damage might be related to the toxicity associated with an increase of Glu, what might be linked with the auditory hallucinations. Finally, the association of these abnormalities with a greater distress caused by auditory hallucinations suggests a failure in the auditory mediated defense system.

References

1. Vercammen A, Knegtering H, Bruggeman R, Aleman A. Subjective loudness and reality of auditory verbal hallucinations and activation of the inner speech processing network. Schizophr Bull 2011; 37: 1009-16.
2. Malmierca MS. The structure and physiology of the rat auditory system: an overview. Int Rev Neurobiol 2003; 56: 147-211.
3. Shergill SS, Brammer MJ, Williams SC, Murray RM, McGuire PK. Mapping auditory hallucinations in schizophrenia using functional magnetic resonance imaging. Arch Gen Psychiatry 2000; 57: 1033-8.
4. Kang DH, Kwon KW, Gu BM, Choi JS, Jang JH, Kwon JS. Structural abnormalities of the right inferior colliculus in schizophrenia. Psychiatry Res 2008; 164: 160-5.
5. Ross AJ, Sachdev PS. Magnetic resonance spectroscopy in cognitive research. Brain Res Brain Res Rev 2004; 44: 83-102.
6. Pirko I, Fricke ST, Johnson AJ, Rodriguez M, Macura SI. Magnetic resonance imaging, microscopy, and spectroscopy of the central nervous system in experimental animals. NeuroRx 2005; 2: 250-64.
7. Miller BL. A review of chemical issues in 1H NMR spectroscopy: N-acetyl-L-aspartate, creatine and choline. NMR Biomed 1991; 4: 47-52.
8. Keshavan MS, Stanley JA, Pettegrew JW. Magnetic resonance spectroscopy in schizophrenia: methodological issues and findings –part II. Biol Psychiatry 2000; 48: 369-80.
9. Martínez-Granados B, Brotons O, Martínez-Bisbal MC, Celda B, Martí-Bonmatí L, Aguilar EJ, et al. Spectroscopic metabolomic abnormalities in the thalamus related to auditory hallucinations in patients with schizophrenia. Schizophr Res 2008; 104: 13-22.
10. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington DC: American Psychiatric Press; 1994.
11. González JC, Sanjuán J, Cañete C, Echanove MJ, Leal C. Evaluation of auditory hallucinations: the PSYRATS scale. Actas Esp Psiquiatr 2003; 31: 10-7.
12. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. Psychol Rep 1962; 10: 799-812.
13. Naressi A, Couturier C, Castang I, De Beer R, Graveron-Demilly D. Java-based graphical user interface for MRUI, a software package for quantitation of in vivo/medical magnetic resonance spectroscopy signals. Comput Biol Med 2001; 31: 269-86.
14. Vanhamme L, Van den Boogaart A, Van Huffel S. Improved method for accurate and efficient quantification of MRS data with use of prior knowledge. J Magn Reson 1997; 129: 35-43.

15. Gajewicz W, Papierz W, Szymczak W, Goraj B. The use of proton MRS in the differential diagnosis of brain tumors and tumor-like processes. Med Sci Monit 2003; 9: MT97-105.
16. Lewis DA, Moghaddam B. Cognitive dysfunction in schizophrenia: convergence of gamma-aminobutyric acid and glutamate alterations. Arch Neurol 2006; 63: 1372-6.
17. Herraiz C. Physiopathological mechanisms in tinnitus generation and persistence. Acta Otorrinolaringol Esp 2005; 56: 335-42.
18. Pujol R, Puel JL. Excitotoxicity, synaptic repair, and functional recovery in the mammalian cochlea: a review of recent findings. Ann N Y Acad Sci 1999; 884: 249-54.
19. Hugdahl K, Loberg EM, Jorgensen HA, Lundervold A, Lund A, Green MF, et al. Left hemisphere lateralisation of auditory hallucinations in schizophrenia: a dichotic listening study. Cogn Neuropsychiatry 2008; 13: 166-79.
20. Grillon C, Ameli R, Charney DS, Krystal J, Braff D. Startle gating deficits occur across prepulse intensities in schizophrenic patients. Biol Psychiatry 1992; 32: 939-43.
21. Li L, Korngut LM, Frost BJ, Beninger RJ. Prepulse inhibition following lesions of the inferior colliculus: prepulse intensity functions. Physiol Behav 1998; 65: 133-9.
22. García-Martí G, Martí-Bonmatí L, Aguilar EJ, Sanz-Requena R, Alberich-Bayarri A, Bonmatí A, et al. Neuroimagen funcional en el estudio de las conductas agresivas en pacientes con esquizofrenia. Rev Neurol 2013; 56: 193-9.
23. Baas JM, Milstein J, Donlevy M, Grillon C. Brainstem correlates of defensive states in humans. Biol Psychiatry 2006; 59: 588-93.
24. Hoffman RE. Revisiting Arieti's 'listening attitude' and hallucinated voices. Schizophr Bull 2010; 36: 440-2.

Estudio del colículo inferior de pacientes con esquizofrenia mediante espectroscopía de resonancia magnética

Introducción. Algunos estudios anteriores en pacientes con esquizofrenia han sugerido alteraciones morfométricas y funcionales en el colículo inferior. Las alucinaciones auditivas son uno de los síntomas centrales en la esquizofrenia. Se piensa que en este evento complejo y multidisciplinar, tanto la atención como la emoción desempeñan un papel clave.

Objetivo. Estudiar los cambios metabólicos en el colículo inferior, un núcleo integrado en la vía auditiva, en pacientes con esquizofrenia y su posible relación con las alucinaciones auditivas.

Sujetos y métodos. Se llevaron a cabo estudios de espectroscopía de resonancia magnética en 30 pacientes diestros con esquizofrenia crónica (19 de ellos con alucinaciones auditivas) y 28 controles. Se adquirió una secuencia 2D de espectroscopía de resonancia magnética y se seleccionaron los vóxeles representativos de ambos colículos inferiores. Se calculó el área de los picos de N-acetilaspartato (NAA), creatina (Cr) y colina (Co).

Resultados. Los pacientes con esquizofrenia mostraron una reducción significativa de NAA/Cr en el colículo inferior derecho comparados con los sujetos control. Los datos metabólicos en el colículo inferior derecho se correlacionaron con los ítems emocionales de las alucinaciones auditivas.

Conclusiones. La contribución del colículo inferior a las bases neuronales de las alucinaciones auditivas es particularmente relevante para el colículo inferior derecho y se centra en el componente atencional-emocional de este síntoma.

Palabras clave. Alucinaciones auditivas. Atención. Colículo inferior. Espectroscopía de resonancia magnética. Esquizofrenia. N-acetilaspartato.