

# AUDITORY GABA CONCENTRATION IS RELATED TO AUDITORY GAMMA-BAND POWER IN NORMAL CONTROLS AND IN AUTISM

Mark S. Brown<sup>1</sup>, Sarah Steinmetz<sup>2</sup>, Susan L. Hepburn<sup>3</sup>, Deb Singel<sup>4</sup>, and Donald C. Rojas<sup>5</sup>

<sup>1</sup>Radiology, University of Colorado Denver, Aurora, CO, United States, <sup>2</sup>University of Colorado Denver, Aurora, CO, United States, <sup>3</sup>Psychiatry & Pediatrics, JFK Partners/University of Colorado School of Medicine, Aurora, CO, United States, <sup>4</sup>Brain Imaging Center, University of Colorado Denver, Aurora, CO, United States, <sup>5</sup>Psychiatry, University of Colorado Denver, Aurora, CO, United States

## **Target Audience**

Researchers and neuroscientists interested in the role of neurotransmitters in healthy subjects and in psychiatric illnesses.

## **Purpose**

Brain gamma band (30-80 Hz) oscillatory activity, measured via EEG and magnetoencephalography (MEG), is thought to be associated with higher brain functions which may become disrupted in psychiatric illnesses. Previously published data demonstrated reduced auditory gamma band power in persons with autism spectrum disorders (ASD)<sup>1,2</sup> and their first degree relatives.<sup>3,4</sup> Gamma band activity has also been shown to correlate with levels of  $\gamma$ -aminobutyric acid (GABA) in animal model studies and in human studies combining MRS and MEG.<sup>5,6</sup> Independently, prior MRS work has suggested reduced GABA in persons with autism.<sup>7-9</sup> Other previous, preliminary work suggested a relationship between auditory gamma-band response and auditory GABA.<sup>10</sup> The relationship between GABA concentration and auditory gamma-band activity has not yet been studied in autism. Here, we examine the relationship between auditory GABA concentration and gamma-band power in individuals with autism and in healthy control subjects.

## **Methods**

Auditory transient and steady-state gamma-band responses and auditory cortical GABA concentration were measured in 2 groups of children and adolescents: a) healthy controls (N=25) and b) people with autism spectrum disorders (N=24). Auditory response data were acquired using a 248-channel whole head magnetoencephalography (MEG) system (Magnes 3600 WH), GABA concentrations were obtained via J-edited <sup>1</sup>H-MRS using a MEGA-PRESS<sup>11</sup> sequence on a GE 3T/94 MRI system (GE Healthcare) as previously described.<sup>8</sup> Measurements were restricted to the left hemisphere due to time constraints of the spectroscopy sequence.

## **Results**

Transient gamma-band power was significantly higher in the control group compared to individuals with autism ( $p < .01$ ). GABA concentration was significantly lower in the autism ( $p < .05$ ) compared with controls. GABA concentration was correlated with transient gamma-band power in the control group ( $r = .45$ ,  $p < .002$ ) and approached significance in the autism group ( $r = .35$ ,  $p = .08$ ). No correlations with steady-state response power and GABA were observed.

## **Discussion**

These results are consistent with our previous preliminary findings of a relationship between gamma band power and GABA levels.<sup>10</sup> They reinforce the suggestion that reduced GABA levels may be related to reductions in stimulus related gamma-band power frequently reported in autism. The finding that the obligatory transient auditory gamma response was associated with GABA while the steady state response was not implies different mechanisms of generation for the two responses. This is consistent with earlier literature suggesting that the steady-state responses reflect the superimposition of mid-latency auditory evoked responses.

## **Conclusions**

GABA concentration and gamma-band power may both be related endophenotypes in autism that are related to an underlying change in inhibitory function.

## **Support**

Supported by NIH/NIMH grants R01 MH082820, R01 MH082820-03S1 and by NIH/NCRR Colorado CTSI grant UL1 RR025780. Contents are the authors' sole responsibility and do not necessarily represent official NIH views.

## **References**

1. Wilson TW, Rojas DC, Reite ML, et al. Children and adolescents with autism exhibit reduced MEG steady-state gamma responses. *Biol.Psychiatry* 2007; 62:192–197.
2. Gandal MJ, Edgar JC, Ehrlichman RS et al. Validating  $\gamma$  oscillations and delayed auditory responses as translational biomarkers of autism. *Biol. Psychiatry* 2010; 68:1100–1106.
3. Rojas DC, Maharajh K, Teale P, et al. Reduced neural synchronization of gamma-band MEG oscillations in first-degree relatives of children with autism. *BMC Psychiatry* 2008; 8: 66.
4. Rojas DC, Teale PD, Maharajh K, et al. 2011. Transient and steady-state auditory gamma band responses in first-degree relatives of people with autism spectrum disorder. *Mol Autism* 2011; 2:11.
5. Muthukumaraswamy SD, Edden RA, Jones DK, et al. Resting GABA concentration predicts peak gamma frequency and fMRI amplitude in response to visual stimulation in humans. *Proc. Natl. Acad. Sci. U. S. A.*, 2009;106:8356–8361.
6. Edden RA, Muthukumaraswamy SD, Freeman TC, et al. *J. Neurosci* 2009;29(50):15721-15726.
7. Harada M, Taki MM, Nose A, et al. 2010. Non-invasive evaluation of the GABAergic/Glutamatergic system in autistic patients observed by MEGA-editing proton MR spectroscopy using a clinical 3 Tesla instrument. *J Autism Dev Disord* 2010; 41:447–454.
8. Rojas DC, Singel D, Steinmetz S, et al., Decreased left perisylvian GABA concentration in children with autism and unaffected siblings, *NeuroImage* (2013), in press.
9. Gaetz, W, Bloy L, Wang DJ, et al., GABA estimation in the brains of children on the autism spectrum: Measurement precision and regional cortical variation, *NeuroImage* (2013), in press.
10. Brown MS, Teale P, Collins D, et al. MEG auditory evoked gamma phase locking correlates with 1H-MRS determined temporal lobe GABA levels. Abstract 6807 Proceedings of 19<sup>th</sup> Annual Meeting, International Society for Magnetic Resonance in Medicine, May 2011, Montreal, ON.
11. Mescher, M., Merkle, H., Kirsch, J., et al. Simultaneous in vivo spectral editing and water suppression. *NMR Biomed* 1998;11:266–272.