

Annual Report 2012-2013

WAKE FOREST UNIVERSITY GRADUATE SCHOOL OF ARTS AND SCIENCES

The poster is titled "Alcohol Withdrawal Seizure Severity is Reduced by Ethosuximide, a T-type Calcium Channel Antagonist" and is presented by Melissa A. Riegler¹, Erin H. Caulder² and Dwayne W. Godwin^{1,2}. The poster is divided into several sections: Introduction, Methods, Results, and Conclusion. The Results section includes four numbered panels: 1. ETX Does Not Impair Motor Function, 2. Spike Wave Discharge Events in DBA/2J Mice, 3. SWDs Increase with Successive WD, and 4. ETX reduces SWD Events During WD. Panel 4 contains bar graphs showing SWD Events for Baseline, WD1, WD2, WD3, and WD4, comparing Saline, 50mg/kg ETX, 100mg/kg ETX, and 250mg/kg ETX treatments. A legend is provided for the bar graphs. The Conclusion section states that ETX did not inhibit decrease in SWD or motor function, seizure activity in the WD period, and ETX decreased seizure activity consistent with T-type calcium channel antagonism. ETX may serve as a potential treatment option during alcohol withdrawal.

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Alcohol Withdrawal Seizure Severity is Reduced by Ethosuximide, a T-type Calcium Channel Antagonist
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INTRODUCTION

- Chronic alcohol abuse depresses the nervous system but abstinence may result in hyperexcitability and seizure. Withdrawal (WD) symptoms, including seizures, drive individuals to relapse and represent a significant barrier to recovery.
- Previous experiments in our lab have identified the thalamic T-type calcium channel (T-channel) isoform $Ca_v2.2$ as a novel target of ethanol. Disruption of T-current may be involved in the generation and propagation of WD seizures.
- We hypothesized that ethosuximide (ETX), a T-channel antagonist used for treatment of generalized epilepsy, might decrease the severity of alcohol WD seizures.

METHODS

- DBA/2J mice were implanted with the Pinnacle, Inc. EEG acquisition system. The EEG headmount was surgically implanted under ketamine/xylazine (100 and 10 mg/kg respectively) anesthesia and mice were allowed 1 week recovery.
- In a vapor chamber, mice were exposed to 4 days of intermittent alcohol. The paradigm consisted of 16 hours of exposure, followed by 8 hours of WD.
- Mice were treated with saline, ETX (50, 100, 250 mg/kg), or lorazepam (1 mg/kg) four and a half hours into each WD period, beginning at peak time of seizure activity (1:30 pm). A separate control group exposed to air only were treated with 250 mg/kg ETX and evaluated.
- Cortical EEG activity was recorded during an 8 hr baseline period prior to exposure and during each 8 hr WD period. Spike wave discharge (SWD) events (6-10 sec) were counted for each mouse and averaged.
- Motor ability was evaluated using a rotarod test.

RESULTS

1 ETX Does Not Impair Motor Function

Figure 1. Rotarod tests were conducted to assess motor function prior to and 15, 30, 60 min, and 3 hours after drug administration. ETX did not impair motor ability. Kruskal-Wallis test with Dunnett's Multiple Comparison test ($n = 4-5$).

2 Spike Wave Discharge Events in DBA/2J Mice

Figure 2. The above trace represents a spike and wave discharge (SWD) event. Cortical EEG activity was recorded during each alcohol WD period. SWD events occur between 8-1400 in DBA/2J mice.

3 SWDs Increase with Successive WD

Figure 3. DBA/2J mice underwent an intermittent alcohol exposure paradigm consisting of 4 exposures (16 hours each) and 4 WDs (8 hours each). SWD events were counted in the last 3 hours of each WD period. In mice treated with saline, we observed an increase in SWD events over successive WD periods. $p < 0.001$. Kruskal-Wallis test with Dunnett's Multiple Comparison test ($n = 5$).

4 ETX reduces SWD Events During WD

Figure 4. During WD, mice were treated at 1:30 pm with saline, ETX (50, 100, 250 mg/kg), or Lorazepam (1 mg/kg). SWD events were counted for the last 3 hours of each WD (2-5 pm) after treatment. There were no differences between groups in baseline values of SWD events. In all WD periods, mice treated with 250 mg/kg ETX had decreased SWD events compared to mice treated with saline. Lower doses of ETX and Lorazepam did not reduce SWDs compared to saline treated mice. $^{*}p < 0.001$, $^{**}p < 0.001$, Kruskal-Wallis test.

5 ETX R...

Figure 5. To determine that had developed in treatment (10:30 am - 11:30 am). Analysis revealed a sig of events prior to and Two-way ANOVA test w...

6 Example

Figure 6. Example spectra during the 4th WD. Power treatment, supporting the time of treatment.

CONCLUSION

- ETX did not inhibit decrease in SWD or motor function.
- Seizure activity in the WD period.
- ETX decreased seizure activity consistent with T-type calcium channel antagonism.
- ETX may serve as a potential treatment option during alcohol withdrawal.

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WAKE FOREST
UNIVERSITY

**Table 1. Application Summary
Fall 2012**

Degree Program	# Applications	# Accepted	# Enrolled
Biomedical Engineering MS	62	4 (6%)	2 (50%)
Biomedical Engineering PhD	139	51 (37%)	30 (59%)
Biomedical Engineering MD/PhD	14		
Clinical and Population Translational Sciences MS	9	6 (67%)	3 (50%)
Comparative Medicine MS			
Integrative Physiology and Pharmacology PhD	39	9 (23%)	5 (56%)
Integrative Physiology and Pharmacology MD/PhD	3	1 (33%)	1 (100%)
Molecular and Cellular Biosciences PhD	247	28 (11%)	14 (50%)
Molecular and Cellular Biosciences MD/PhD	37	3 (8%)	1 (33%)
Neuroscience PhD	101	15 (15%)	6 (40%)
Neuroscience MD/PhD	17	2 (12%)	1 (50%)
TOTAL	668	119 (18%)	63 (53%)

Table 2. Applicant Profile
Fall 2012

Degree Program	Male	Female	Not Reported	TOTAL	American Indian/ Alaska Native	Asian	Black or African American	Hispanic / Latino	Native Hawaiian/ Pacific Islander	White	Two or More Races	Non-resident Alien	Not Reported
Biomedical Engineering MS	25	36	1	62		5	1			25		31	
Biomedical Engineering PhD	72	64	3	139		20	3	2		56	3	51	4
Biomedical Engineering MD/PhD	12	2		14		2				11			1
Clinical and Population Translational Sciences MS	3	6		9		2				6	1		
Comparative Medicine MS													
Integrative Physiology and Pharmacology PhD	18	21		39				2		15	1	19	2
Integrative Physiology and Pharmacology MD/PhD	2	1		3		1		1		1			
Molecular and Cellular Biosciences PhD	109	138		247	1	11	18	7		93	3	110	4
Molecular and Cellular Biosciences MD/PhD	26	11		37		5	2	4		23			3
Neuroscience PhD	50	51		101	1	6	6	3		54	1	23	7
Neuroscience MD/PhD	10	7		17		2	1	1		11			2
TOTAL	327	337	4	668	2	54	31	20		295	9	234	23

**Table 3. Applicant Average Test Scores and GPA
Fall 2012**

Degree Program	GRE Verbal	GRE Quantitative	(V+Q)	GRE Analytical	GPA	TOEFL	MCAT
Biomedical Engineering MS	154	159	313	3.8	3.3	103	
Biomedical Engineering PhD	156	161	317	4.1	3.6	97	
Biomedical Engineering MD/PhD					3.7		34
Clinical and Population Translational Sciences MS	153	148	301	4.5	3.5		
Comparative Medicine MS							
Integrative Physiology and Pharmacology PhD	153	155	308	3.6	3.4	104	
Integrative Physiology and Pharmacology MD/PhD					3.8		32
Molecular and Cellular Biosciences PhD	155	156	311	3.7	3.4	99	
Molecular and Cellular Biosciences MD/PhD					3.8		34
Neuroscience PhD	157	156	313	4.1	3.4	95	
Neuroscience MD/PhD					3.8		34
AVERAGE	155	157	312	3.9	3.4	99	32

Table 4. Accepted Student Profile
Fall 2012

Degree Program	Male	Female	Not Reported	TOTAL	American Indian/ Alaska Native	Asian	Black or African American	Hispanic / Latino	Native Hawaiian/ Pacific Islander	White	Two or More Races	Non-resident Alien	Not Reported
Biomedical Engineering MS		4		4						4			
Biomedical Engineering PhD	22	29		51		5	2	2		27	2	11	2
Biomedical Engineering MD/PhD													
Clinical and Population Translational Sciences MS	2	4		6						6			
Comparative Medicine MS													
Integrative Physiology and Pharmacology PhD	5	4		9				1		4		3	1
Integrative Physiology and Pharmacology MD/PhD		1		1		1							
Molecular and Cellular Biosciences PhD	9	19		28	1		3			18		5	1
Molecular and Cellular Biosciences MD/PhD	3			3			1			1			1
Neuroscience PhD	6	9		15	1			1		8		1	4
Neuroscience MD/PhD	1	1		2						1			1
TOTAL	48	71		119	2	6	6	4		69	2	20	10

**Table 5. Accepted Student Average Test Scores and GPA
Fall 2012**

Degree Program	GRE Verbal	GRE Quantitative	(V+Q)	GRE Analytical	GPA	TOEFL	MCAT
Biomedical Engineering MS	160	160	320	4.6	3.6		
Biomedical Engineering PhD	156	160	316	4.3	3.6	105	
Biomedical Engineering MD/PhD							
Clinical and Population Translational Sciences MS	151	147	298	4.5	3.5		
Comparative Medicine MS							
Integrative Physiology and Pharmacology PhD	156	156	312	3.9	3.6	91	
Integrative Physiology and Pharmacology MD/PhD							36
Molecular and Cellular Biosciences PhD	157	157	314	4.2	3.6	111	
Molecular and Cellular Biosciences MD/PhD							37
Neuroscience PhD	162	159	321	4.6	3.5		
Neuroscience MD/PhD							35
AVERAGE	157	158	315	4.3	3.5	103	30

Table 6. Matriculated Student Profile
Fall 2012

Degree Program	Male	Female	Not Reported	TOTAL	American Indian/ Alaska Native	Asian	Black or African American	Hispanic / Latino	Native Hawaiian/ Pacific Islander	White	Two or More Races	Non-resident Alien	Not Reported
Biomedical Engineering MS		2		2						2			
Biomedical Engineering PhD	11	19		30		2	3	1		18	1	5	
Biomedical Engineering MD/PhD													
Clinical and Population Translational Sciences MS	1	2		3						3			
Comparative Medicine MS													
Integrative Physiology and Pharmacology PhD	3	2		5						3		2	
Integrative Physiology and Pharmacology MD/PhD		1		1		1							
Molecular and Cellular Biosciences PhD	4	10		14	1		2			9		2	
Molecular and Cellular Biosciences MD/PhD	1			1						1			
Neuroscience PhD	3	3		6	1					2		1	2
Neuroscience MD/PhD		1		1									1
TOTAL	23	40		63	2	3	5	1		38	1	10	3

**Table 7. Matriculated Student Average Test Scores and GPA
Fall 2012**

Degree Program	GRE Verbal	GRE Quantitative	(V+Q)	GRE Analytical	GPA	TOEFL	MCAT
Biomedical Engineering MS	164	158	322	4.8	3.4		
Biomedical Engineering PhD	156	160	316	4.3	3.6	103	
Biomedical Engineering MD/PhD							
Clinical and Population Translational Sciences MS	148	149	297	4.5	3.6		
Comparative Medicine MS							
Integrative Physiology and Pharmacology PhD	159	160	319	4.1	3.5	91	
Integrative Physiology and Pharmacology MD/PhD							36
Molecular and Cellular Biosciences PhD	156	155	311	4.1	3.6		
Molecular and Cellular Biosciences MD/PhD							40
Neuroscience PhD	161	158	319	4.3	3.5		
Neuroscience MD/PhD							32
AVERAGE	157	158	315	4.3	3.5	99	29

**Table 8. Student Enrollment by Program and Degree
Fall 2012**

Degree Program	PhD	MD/PhD	MS	Unclassified	TOTAL
Biochemistry and Molecular Biology	16	1			17
Biomedical Engineering - WFU	39		2		41
Biomedical Engineering - VT	66		7		73
Cancer Biology	16				16
Clinical and Population Translational Sciences			23		23
Comparative Medicine					
Integrative Physiology and Pharmacology	21				21
Microbiology and Immunology	15	1			16
Molecular and Cellular Biosciences	14				14
Molecular Genetics and Genomics	14				14
Molecular Medicine and Translational Science	22	1	1		24
Molecular Pathology	18				18
Neurobiology and Anatomy	4				4
Neuroscience	40	1			41
Unclassified				25	25
TOTAL	285	4	33	25	347

**Table 9. Registered Student Profile
Fall 2012**

Degree Program	Amer Indian/ Alaska Native		Asian		Black or African American		Hispanic/Latino		Native Hawaiian/ Pacific Islander		White		Two or More Races		Non-resident Alien		Unknown		TOTAL
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
Biochemistry and Molecular Biology											5	10				2			17
Biomedical Engineering			3	3	4	2					30	50			13	9			114
Cancer Biology			1	1		2					5	6				1			16
Clinical and Population Translational Sciences					1						9	9			2		2		23
Comparative Medicine																			
Integrative Physiology and Pharmacology											9	5			4	3			21
Microbiology and Immunology						2							5	6		1	1	1	16
Molecular and Cellular Biosciences	1					2					2	7			1	1			14
Molecular Genetics and Genomics											5	5			2		1	1	14
Molecular Medicine and Translational Science			1	2	1	1					8	6			2	2	1		24
Molecular Pathology						2					3	7			2	3	1		18
Neurobiology and Anatomy											1	2				1			4
Neuroscience		1									15	18			3	1	1	2	41
MD/PhD§											2	1				1			4
TOTAL	1	1	5	6	6	11	0	0	0	0	92	125	5	6	29	24	7	4	322

§Not included in totals - already counted in programs of study

**Table 10. International Enrolled New Student Profile
Fall 2012**

Degree Program	Barbados	Cameroon	Canada	China	Colombia	Germany	Guyana	India	Indonesia	Iran	Israel	Jordan	Pakistan	Russian Federation	Taiwan	Total
Biomedical Engineering				2												2
Clinical and Population Translational Science																
Comparative Medicine																
Integrative Physiology and Pharmacology				1												1
Molecular and Cellular Biosciences				1				1								2
Neuroscience														1		1
TOTAL				4				1						1		6

**Table 11. International Registered Student Profile
Fall 2012**

Degree Program	Barbados	Cameroon	Canada	China	Colombia	Germany	Guyana	India	Indonesia	Iran	Israel	Jordan	Pakistan	Russian Federation	Taiwan	Total
Biochemistry and Molecular Biology				1			1									2
Biomedical Engineering				6				1			1					8
Cancer Biology				1												1
Clinical and Population Translational Science		1											1			2
Comparative Medicine																
Integrative Physiology and Pharmacology	1		1	2				2				1				7
Microbiology and Immunology					1											1
Molecular and Cellular Biosciences				1				1								2
Molecular Genetics and Genomics								1	1							2
Molecular Medicine and Translational Science				1		1				1					1	4
Molecular Pathology				4					1							5
Neurobiology and Anatomy				1												1
Neuroscience						1		1			1			1		4
TOTAL	1	1	1	17	1	2	1	6	2	1	2	1	1	1	1	39

Table 12. Financial Aid Summary
Fall 2012

Degree Program	Institutional Support			External Support			Self	Other	TOTAL
	Graduate Fellowship	Non-grad Institutional	Teaching Assistantship	Individual Award	Research Grant	Training Grant			
Biochemistry and Molecular Biology			1		14	2			17
Biomedical Engineering - WFU	5			5	30		1		41
Biomedical Engineering - VT§									0
Cancer Biology		4			5	6	1		16
Clinical and Population Translational Sciences***		1*				8**	14		23
Comparative Medicine									0
Integrative Physiology and Pharmacology	5	1		1	10	1		3	21
Microbiology and Immunology				1	10	5			16
Molecular and Cellular Biosciences	14								14
Molecular Genetics and Genomics			1		12			1	14
Molecular Medicine and Translational Science					19	1	1	3	24
Molecular Pathology				2	8	5	3		18
Neurobiology and Anatomy					3	1			4
Neuroscience	9		1	7	10	11	1	2	41
Unclassified***		5				8	12		25
TOTAL	33	11	3	16	121	48	33	9	274

§Virginia Tech support information not available

*Tuition was funded by graduate and non-graduate institutional funds

**Tuition was funded by graduate and training grant funds

***Tuition Only

TABLE 13. DEGREES AWARDED BY PROGRAM AND DEGREE

CLASS OF 2012-2013

	PhD Programs			Masters Programs	TOTAL
	PhD	MS	MD/PhD		
Biochemistry and Molecular Biology	4				4
Biomedical Engineering - WFU	2	2		3	7
Biomedical Engineering - VT	9			4	13
Cancer Biology	5	1			6
Clinical and Population Translational Sciences				5	5
Comparative Medicine					0
Integrative Physiology and Pharmacology	2				2
Microbiology and Immunology	1				1
Molecular and Cellular Biosciences					0
Molecular Genetics and Genomics	3				3
Molecular Medicine and Translational Science	4	1			5
Molecular Pathology	8				8
Neurobiology and Anatomy	3				3
Neuroscience	6	1			7
TOTAL	47	5		12	64

TABLE 14. TIME TO DEGREE BY PROGRAM, CLASS OF 2012-2013

	PhD	MS
Biochemistry and Molecular Biology	4.75	
Biomedical Engineering	5.16	1.80
Cancer Biology	5.66	4.00
Clinical and Population Translational Sciences		2.33
Comparative Medicine		
Integrative Physiology and Pharmacology	5.00	
Microbiology and Immunology	4.33	
Molecular Genetics and Genomics	5.33	
Molecular Medicine and Translational Science	5.08	3.33
Molecular Pathology	5.33	
Neurobiology and Anatomy	6.55	
Neuroscience	5.05	3.00
AVERAGE	5.22	2.89

*Average of years from matriculation to awarding of the degree

TABLE 15. PLACEMENT BY PROGRAM, UNDERGRADUATE INSTITUTION, DEGREE, AND PLANS, 2012-2013, AY

Program	Undergraduate Institution	Degree	Plans
BAMB	DePauw University	PhD	Post Doc, Harvard Medical School
	Guilford College		Post Doc, National Institute of Environmental Health Sciences, Research Triangle Park, NC
	Otterbein College		Post Doc, Ohio State University Medical Center
	Virginia Union University		Post Doc, Location Unknown
BMES	North Carolina State University	PhD	Biomedical Engineer Researcher, Altus Engineering
	Western New England University		Scientist, Starlight Insights
	North Carolina State University	MS	Research & Product Development Engineer, Cook Medical
	Virginia Tech		Research & Development Engineer, Johns Hopkins University
CABI	Guangxi Medical University	PhD	Internal Medicine Resident, Englewood Hospital
	Guru Gobind Singh Indraprastha Univ.		Post Doc, Duke Eye Center
	Kennesaw State University		Post Doc, Scripps Institute
	UNC – Chapel Hill		Post Doc, Unknown
	Ursinus College		Intern, Medical Oncology, Greater Baltimore Medical Center
	Elon University	MS	Lab Tech, WFBHS
CPTS	Government College Lahore Pakistan	MS	Phlebology Fellowship, New York University
	James Madison University		Research, WFBHS
	Kenyon College		Assistant Professor, WFBHS
	University of Yaounde 1		Pursue PhD, Vanderbilt University
	Wake Forest University		Pursue PhD in Human Development & Family Studies, UNC-Greensboro
IPP	Ohio Northern University	PhD	Pharmacist & Research Liaison, Walter Reed National Military Medical Center
	University of Wisconsin - Oshkosh		Post Doc, Rosalind Franklin University
MICR	Appalachian State University	PhD	Teaching Fellowship, Virginia Commonwealth University
MOGN	Andhra University	PhD	Commercialization Associate, Wake Forest Innovations
	University of Calcutta		Post Doc, WFBHS
	University of Illinois		Unknown
MMTS	University of Georgia	PhD	Post Doc, Vanderbilt University
	University of Maine		Post Doc, Jackson Labs
	UNC-Greensboro		Post Doc, Virginia Tech
	Winthrop University		Post Doc, Vanderbilt University
	Shorter College	MS	Pursue PhD in Regenerative Medicine, UNC-Chapel Hill

TABLE 15. PLACEMENT BY PROGRAM, UNDERGRADUATE INSTITUTION, DEGREE, AND PLANS, 2012-2013, AY

MCPA	Bob Jones University	PhD	Post Doc, University of Texas, Southwestern
	Emory & Henry College		Post Doc, WFBHS
	Fudan University		Post Doc, University of Texas, Southwestern
	North Carolina State University		Analyst for Security Management Company
	University of Georgia		Post Doc, Cleveland Clinic
MCPA	Wake Forest University	PhD	Freelance Editor
	Wuhan University		Program Chair, Veterinary Training Program, Sanford Brown College
			Post Doc, WFBHS
NBAT	Appalachian State University	PhD	Assistant Program Manager, WFBHS
	Madras University		Post Doc, University of California, San Francisco
	National University of Cordoba		Post Doc, WFBHS
NEUR	College of William & Mary	PhD	Post Doc, University of Florida
	East Carolina University		Post Doc, WFBHS
	James Madison University		Post Doc, WFBHS
	Louisiana Tech University		Medical Science Liaison, Allergan
	Purdue University		Post Doc, WFBHS
	Tulane University	Post Doc, University of Pennsylvania	
NEUR	UNC-Greensboro	MS	Pursue PhD in Counseling, UNC-Greensboro

TABLE 16. DEGREE COMPLETION RATES

Masters - Fall 2011

PhD - Fall 2006

	Matriculated		Graduated		% Completion	
	PhD	MS	PhD	MS	PhD	MS
Biochemistry and Molecular Biology	4		4		100%	
Biomedical Engineering	4	1	4	1	100%	100%
Cancer Biology	7		6		86%	
Clinical and Population Translational Sciences		11				
Comparative Medicine						
Integrative Physiology and Pharmacology	5		4		80%	
Microbiology and Immunology	6		4		67%	
Molecular Genetics and Genomics	5		4		80%	
Molecular Medicine and Translational Science	3		2		67%	
Molecular Pathology	6		5		83%	
Neurobiology and Anatomy	5		4		80%	
Neuroscience	5		3		60%	
TOTAL	50	12	40	1	80%	100%