30 Years of Accepted Science of the NeuroGuide Normative Databases

In 1979, Robert W. Thatcher, Ph.D. was a professor at the University of Maryland and he was the principal investigator of a project to correlate nutrition and environmental toxins and human brain development from which over 1,350 EEG recordings were obtained. From this total population approx. 620 healthy normal control subjects were identified based on neuropsychological and neurological questionnaires and interviews. This is the same reference normal database used inside of NeuroGuide. In the last five years more adult carefully screened normal subjects were added to the reference database so that total sample size N = 727 and spans the age range from 2 months to 82 years. The database was fit to a Gaussian distribution and cross-validated and the results published in various journals. Because of the 30year history and the number of replications and cross- validations the Univ. of Maryland normative database is considered as accepted science used repeatedly in hundreds of studies over this 30 year period of time, including the National Institutes of Health, the Department of Defense and VA medical centers and universities throughout the world. It has been used in many studies that are independent of Robert Thatcher, Ph.D. (the PI responsible for the database) and there has not been a single study that has refuted the findings in the normative database. This is important because after 30 years of published science that has been tested and independently evaluated and, importantly, without a single study that has refuted the database by comparisons to a different database. No database is perfect, they all are simply statistical references but adherence to scientific standards and mathematical standards is essential for all clinical databases and qEEG is no different. (see Thatcher and Lubar, 2008).

As explained in Thatcher and Lubar (2008) there are two primary methods of reference database construction: 1- Stratification of means & standard deviations by age groups and, 2- Polynomial regression fits across age. The regression fit has the drawback of accounting for a small percentage of the variance across age and a failure to quantify growth spurts (e.g., age 5-7 language development, or age 9-11 of formal operations or 11- 14 for puberty, etc.). The age stratification requires a larger population than the regression method and overlapping of age groups in order to minimize jumps between age groups. The University of Maryland reference normative database has a large number of younger age individuals, especially age 3 to 15 which allowed for one year overlapping and smooth developmental trajectories. The adult age range had a lower sample size, e.g., about 150 subjects and requires creating 10 year age groups with five year overlaps resulting in small (e.g., about 0.5 st. dev.) jumps between these larger age ranges. Recently, the addition of about 180 new subjects giving rise to a total population size of over 900 subjects has provided for greater age overlap of groups and further reduction of jumps as one advances age.

In 2004, the NeuroGuide normative database was determined to comply with FDA standards for a 510K (K041263) registration. FDA registration involved extensive validation and verification tests as well as showing similarity to other normative databases such as the FDA registered NxLink QEEG normative database.

In 2004, a Joint-Time-Frequency-Analysis (JTFA) Hilbert transform was used to compute "Instantaneous" power, coherence and phase values in which auto and cross-

spectra are computed at each time sample in about one microsecond, hence the term "Instantaneous". The same subjects as used in the FFT norms in which means are computed across age groups was used for the Instantaneous means and standard deviations. The instantaneous means and standard deviations involved summing the auto and cross spectral values at each instant of time over the entire EEG recording for all subjects within a given age group and then dividing by the total number of samples which was many thousands of values. The JTFA values are different than FFT values and the method of computing the means and standard deviations for the JTFA norms are different than the method of computing the FFT norms and the means and standard deviation of the FFT norms cannot be used to compute Z scores based on instantaneous values or vice versa. To do so introduces error because of the fundamentals of statistical sampling theory. Analyses show a range of error from 8% to 14% if the mean of a FFT with windowing is used to compute a Z score based on a JTFA calculation of instantaneous frequency. The FFT and JTFA are mathematically different which is one source of the error. The method used by the NeuroGuide database is JTFA means and standard deviations to compute JTFA instantaneous Z scores. This method has zero digital signal processing difference and therefore it is more accurate.

In 2007 an independent cross-validation of the New York University and the University of Maryland FFT age based normative databases were conducted. The study was conducted because a company had collected raw digital EEG from several hundred clinical patients and had computed Z scores using the New York University (NYU) normative database (John, 1977; John et al, 1977; 1987; 1988). The question was: does the University of Maryland (UM) normative database produce similar of comparable Z scores as the NYU database using the same exact raw digital data? The correlation coefficients from the independent cross- validation between the NYU and UM normative databases is shown in the figure below. The analysis included 332 psychiatric patients and an age range from 6.2 years to 84.9 years.

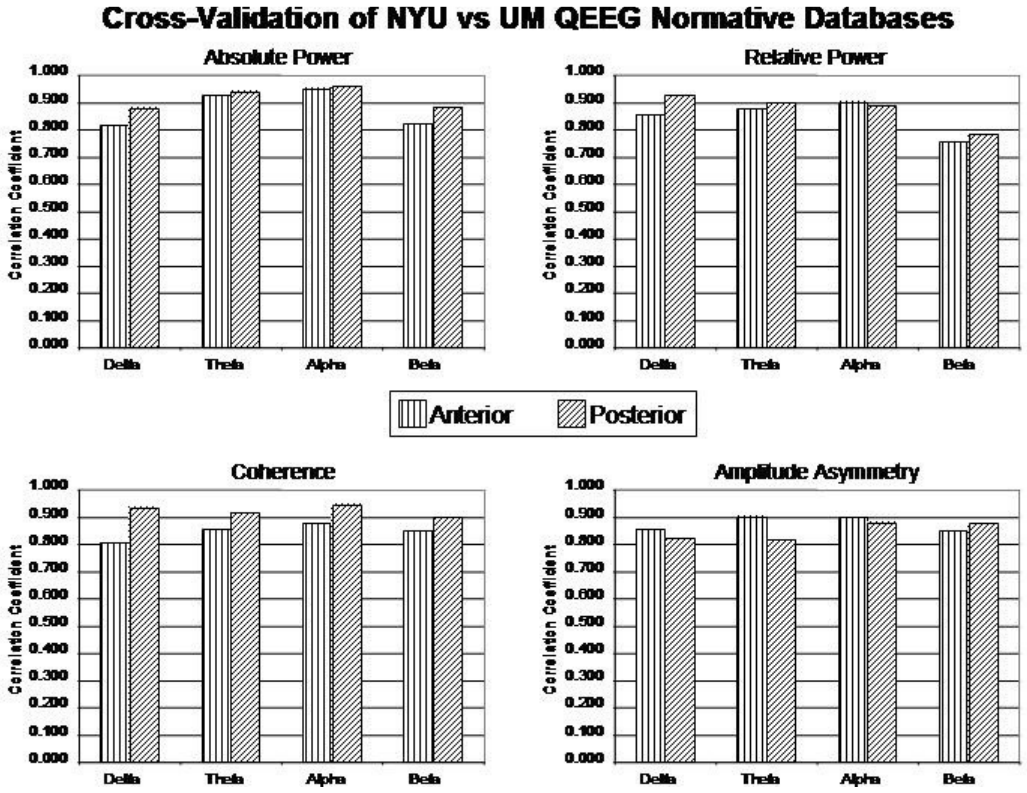

Fig. 1 – Results of an independent cross-validation comparison of Z scores from 332 psychiatric patients ranging in age from 6.2 years to 84.9 years using the NYU and UM normative databases. Anterior and posterior refers to the anterior and posterior location of electrodes. Highly significant independent cross-validation was observed which shows the high degree of consistency between two peer reviewed and clinically validated QEEG normative databases. (Reprinted with permission from Brian McDonald, CNS Response, Inc.

The list below includes some replication studies by Thatcher et al and other scientists as collaborators. These are primarily department of defense funded medical doctors and scientists to evaluate the database for evaluation and treatment of brain injured individuals. The studies by van Baal, and van Beijsterveldt et al are genetic studies that replicated the normative database growth spurts and showed that both environmental and genetic factors are operating in the development of the human brain as measured in the normative database.

Below is a partial list of national and international universities and medical centers that are using the Univ. of Maryland normative database each day of the week in the evaluation of patients with neurological and psychiatric problems.

Cross-Validation and Reliability Tests of the Normative Database

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Thatcher, R.W., Biver, C. J., and North, D. Intelligence and EEG current density using Low Resolution Electromagnetic Tomography, Human Brain Mapping, 2007, 28(2): 118 – 133.

Thatcher, R.W., North, D., and Biver, C. Development of cortical connectivity as

measured by EEG coherence and phase. Human Brain Mapp., 2008, 12:1400-1415.

Thatcher, R.W. and Lubar, J.F. History of the scientific standards of QEEG normative databases. In: Introduction to QEEG and Neurofeedback: Advanced Theory and Applications, T. Budzinsky, H. Budzinsky, J. Evans and A. Abarbanel (eds)., Academic Press, San Diego, CA, 2008.

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Partial List of Independent Evaluations of the Normative Database with No Studies that Have Refuted the Database in the Last 30 Years

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M. Besenyeia, E. Vargab, I. Feketec,∗, S. Puskásc, K. Hollódyd, A. Fogarasie, M. Emrif, G. Oppositsf, S.A. Kis f, B. Clemens. (2012). EEG background activity is abnormal in the temporal and inferior parietal cortex in benign rolandic epilepsy of childhood: A LORETA study. Epilepsy Research (2012) 98, 44—49

B. Clemens, M. Bessenyei a, I. Fekete b, S. Puskás b, I. Kondákor c, M. Tóth d, K. Hollódy (2010). Theta EEG source localization using LORETA in partial epilepsy patients with and without medication. Clinical Neurophysiology 121 (2010) 848– 858.

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Huang-Storms, Lark, Bodenhamer-Davis, Eugenia, Davis, Richard and Dunn, Janice (2007) 'QEEG Guided Neurofeedback for Children with Histories of Abuse and Neglect: Neurodevelopmental Rationale and Pilot Study', Journal of Neurotherapy, 10: 4, 3— 16

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Some of the Universities and Institutions that Use the Normative Database:

Departments of Psychiatry and Neurology, University of Iowa School of Medicine, Iowa City, IA

Department of Psychiatry, Wayne State Medical Center, Detroit, MI

Department of Psychology, University of California at San Diego, CA

College of Business Administration, California State University, Sacramento, CA

Departments of Psychiatry and Behavioral Science, Konkuk University School of Medicine, Seoul, Korea

Department of Nuclear and Quantum Engineering, KAIST 305-701, Guseong-dong, South Korea

Department of Neuropsychiatry, Konkuk University Hospital, 4-12 Hwayang-dong Gwangjin-gu, Seoul Korea

Korea Advanced Instuitute of Science and Technology (KAIST), Seoul Korea

Gyeongsang National University Hospital, Seoul Korea

Presbyterian Medical Center-Jesus Hospital, Seoul Korea

Olda MNB Korea Medical Hospital, Gwangjusi, Korea

Dept. of Psychology, School of Human Sciences, University of Wales, Swansea, UK

Dept. of Psychology, Brown University, Providence, RI

Dept. of Epidemiology, Stanford University, Palo Alto, CA

Department of Psychiatry, School of Medicine, University of Missouri-Kansas City

Dept. of Cognitive & Biological Psychology, Vrije Universiteit Brussel, Pleinlaan 2, Brussels, Belgium

Department of Psychology, Drexel University, Philadelphia, PA

Department of Psychology, Norwegian University of Science & Technology, Trondheim, Norway

University of North Texas, Denton, Texas

VA Medical Center, McGuire Research Institute, Research Service, Richmond, VA

VA Medical Center , Richmond , VA

VA Medical Center, Behavior Medicine, Marion, IL

VA Medical Center, Overton Brooks, Shreveport, LA

VA Medical Center, Division of Biological Neurosciences, Hines, IL

VA Medical Center (VHAJAC), Neurodiagnostics, Jackson , MS

VA Medical Center VISN 17 Center of Excellence For Research on Returning War Veterans, Waco, TX

VA Medical Center, Cheyenne Vet Center, Cheyenne, WY

VA Medical Center, Department of Veterans Affairs, Austin, Texas

Fort Carson US Army Military Base, Colorado Springs, CO

Henry Jackson Foundation, Washington , D.C.

Fort Bliss Army Hospital, El Paso, TX

Integrative Medicine, National Intrepid Center of Excellence, Walter Reed National Military Medical Center

Camp Lejeune, USMC and Landsdorf Army Hospital, Germany

Landsuhl Army Hospital, CTR DE USA Medcom LRMC, Germany

Fort Campbell Warrior Resiliency and Recovery Center, Army Brain Injury Center , Fort Campbell , Kentucky

Malcolm Grow Medical Clinic, Andrews Air Force Base, MD

Military Medical Academy, University Hospital, Sofia, Bulgaria

MacDill Air Force Base, Tampa, Fl

Department of Business Education, Arizona State University, Phoenix, AZ

Beer Sheva Mental Health Center, Hazadik Miroshalim, Beer Sheva, Israel

Sociedad de Neurofisiologia Clinica, Hospital Espanol de Mexico, Mexico City, Mexico

Department of Psychology, Drexel University, Philadelphia, PA

Department of Psychiatry, Korea University Ansan Hospital, South Korea

Biological Sciences Department, Michigan Tech University, Houghton, MI

Department of Psychology, Univ. of Tennessee, Nashville, TN

Department of Rehabilitative Medicine, University of Utah School of Medicine, Salt Lake City, UT

Département de Psychologie Université de Montréal, Montreal, Quebec, Canada

Fundacja Wspierania Rozwoju Kliniki Psychiatrycznej, Akademii Medycznej, Warszawie, Poland

Institute for Basic Research in Developmental Disabilities, Staten Island, New York

Department of Psychology, University of Alberta, Edmonton, Canada

Department of Psychology, Kettering University, Flint, MI

Jiangsu University, China

Capital Institute of Physical Education, China

The Hong Kong Polytechnic University, Hong Kong, China

Department of Psychology, University of Central Missouri, Warrensburg, MO

Neuroscience Department, Columbia University , New York

Translational Neuroscience MIND Research Network, Albuquerque , NM

UNIVERSITÉ DU QUÉBEC, C.P. 500, Trois−Rivières (Québec)

Ammar ebn Yasser, Military Academy, Heliopoles, Cairo EGYPT

Zanjan University of Medical Sciences in Iran

Ross Hyslop, Wuttke, Institute, Scotland

Tarbiat Modares University, Iran

Shahid Beheshti University, Iran

Ahwaz Azad University, Iran

Kerman Neuroscience Research Center, Iran

Institute for Cognitive Science Studies, Iran

Tehran University, Iran

Shiraz Medical Science University, Iran

University of Social Welfare and Rehabilitation Sciences, Iran

Payam-e-Noor University, Iran

Ferdowsi University of Mashhad, Iran

Iran Medical Sciences University, Iran

Warszawski Uniwersytet Medyczyny ul. Zwirki I Wigury, Warszawa

UNAM-JURIQUILLA, JURIQUILLA, QRO. MEXICO

University Putra , Malaysia Timbalan Pengarah Institut Teknologi Maju (ITMA) Serdang Selangor 43400 MALAYSIA

Center for the Army Profession and Ethics, U.S. Army Training and Doctrine Command, West Point, New York

Polytrauma Support Clinic, Tennessee Valley Health System, Nashville, Tennessee

School of Business , St. Bonaventrue University, St. Bonaventure , NY

Advanced Brain Monitoring, Carlsbad, CA

Hanyang University, Seoul, South Korea

Ajou University Hospital Dept. of Otolaryngology, sleep clinic, San5, Wonchon-dong, Yeongtong-gu, Suwon 443-380, Korea

Lev-Hasharon Mental Health Center, POB 90000 Netanya, Israel

EEG and Sleep Laboratory, Prague Psychiatric Center/ National Institute of Mental Health, Czech Republic

United Graduate School of Child Development, Osaka University, Japan

Kyung Hee University Medical Center, Japan

Department of Psychiatry, NYU School of Medicine, New York, New York

UHAMKA-Jakarta Hospital, Indonesia

Neuro-Rehabilitation, Caron Renaissance, Boca Raton, Fl

Caron Treatment Centers, Comprehensive Addiction Treatment, Wernersville Campus, Pennsylvania

Dept. of Functional Neurology, Murdoch University, Perth, Australia
Osaka University, Japan

Erada Centre for Treatment and Rehab, DIAC, Dubai

Unity Behavioral Health, Drug and Addiction Rehabilitation Facilities, Boca Raton, Florida

Neuromodulation Lab, Lev-Hasharon Mental Health Medical Center Israel

Partial list of Cases that QEEG and Normative Database Analyses were Admitted as Evidence in Court for Civil and Criminal Cases

Donna Morrell v Calli & Ricci, Cause No. 227,520, County Court at Law No. 1, Travis County, Texas. Trial in February 1999. Mr. Earl Staelin, 512-322-0355, estaelin@aol.com

Charles Piersol v A-1 Aviation, Inc & Delton E. Macy. Case No. 96-2-02731-1. Superior Court, State of Washington County of Spokane, WA. Mr. William Maxey, 1835 W. Broadway, Spokane, Washington 99201. Trial in September 1999.

Onda Morin v. State Farm Insurance Co., Sarasota County Court, Trial January 1996.

Yolanda Martinez v. State Farm Mutual Automobile Insurance Co. & Frederick A. Lewis, Jr., M.D.. Danny R. Hemphill, Esq., Fest, Jessel & Hemphill, LLC 4150 Darley Avenue, Suite 7, Boulder, CO 80303-6537. Trial was in late 1994 or early 1995.

Vizza v. American Consumers Products, et al. John P. Flaherty, Jr., Esq. Congdon, Flaherty O'Callaghan, Reid Donlon, Travis & Fishlinger, 377 Oak Street, Garden City, New York 11530. Trial was in 1995.

Rebecca Jimenez v. Orlando Transportation, LTD and Mark A. Coney. Case No. CI 95-7732. Circuit Court for Orange County, Fl. 1996.

Alan J. Cross and Betty L. Cross v. Pamela H. Crowell. Et al. File No.: 94-930 Felecia Grossman Ziegler, Esq. 20 North Orange Avenue, Suite 406, P.O. Box 2127, Orlando, Florida 32802- 2127. Trial in Orlando April 1996.

Kathleen G. Martin vs Hubba Hubba's Great American Diner, Inc. And Davis-Latham Construction, Inc. Helene Bergman, Esq., 2000 E. Lamar Blvd., Ste. 530, Arlington, TX 76006. Trial in Fort Worth Texas, 1996.

Bernie Entringer, f/k/a Bernie Butcher vs. Deer Mountain Ski Area Inc. Civ. No. 98-549. Rapid City, Sourh Dakota, Feb. 2000 James P. Hurley, Counsel for Plaintiff.

State of Florida (Plaintiff) vs. Samuel Harris (Defendant), Case No.: 05-2001-CF-041393-AXXX- XX, Kissamee, Fl, Circuit Court of the 18th Judicial circuit, June, 2004

David O'Neil vs. Exit 63 Development, LLC, Island Nursing and Rehabilitation Center, Inc. and Tritec Building Co., Inc., Supreme Court of the State of New York, County of Suffolk, April 24, 2007 – Frye Hearning, QEEG admitted at trial

Perkins v. Erickson and Sea Tech Construction, Inc., Case No. 02-012638(18), Circuit Court of the 17th Judicial Circuit in Broward County, Florida, May 9, 2007 – Frye Hearing, QEEG admitted at trial

Rita Davis, Don Davis, and Rita Davis next friend of Glatin Davis a minor, plaintiffs, vs. Steven Davis, Heartland Express, Inc. of Iowa, and Heartland Express, Inc., defendants. In the Iowa District Court for Henry County, Mt. Pleasant, Iowa, No LALA 010663. Judgment & Order February 22, 2007. (Dr. Tom Matthews was the expert witness).

Kimberly Sullivan vs. Ercan Murat Goksan, Airborne Freight Corp. and Jerome Lazarus, Supreme Court of the State of New York County of Bronx, - QEEG admitted after a Frye Hearing, Case #1-4/27/2005

Meralie A. Dodge vs Dale R. Carpenter et al, Case No. BC 163 482, Superior Court of the State of California, County of Los Angeles, 1998. Edward Steinbrecher, esq. Counsel for Plaintiff.

People v. Musselwhite, 17 Cal.4th 1216 (1998)

People v. Crittender, 9 Cal. 4th 83 (1995).

Marshal v. Branch, Circuit Court of the State of Oregon for Jackson County, Case No. 04-0993-L- 3, 2008.

Rafael Caba vs City of New York, Department of Sanitation, City of New York, Brian Agustan Hale and Freddy A. Rosa. Supreme Court of the State of New York County of Queens, QEEG admitted after a Frye Hearing. 2008. Case No. 24374/04.

Gabriel Steif and Eva Steif plaintiff vs. Greyhound lines, Inc and William Lee Henley, Jr., defendant. United State Federal District Court, Southern District of New York docket # 08 cv 2892 Hon. Judge Maomi Buckwald. February 10, 2009.

State of Florida v. Grady Nelson, Case No. F05-00846, 11th Judicial Circuit Court, Miami-Dade County, Florida. October 22, 2010. QEEG admitted in the penalty phase after a Frye Hearing.

Richard Sawaski v. Gigs, LLC, and Wendell L. Zorman. C.A. No. 08-2380. Commonwealth of Massachusetts. QEEG admitted after a Frye Hearing and Granted Plaintiff's motion to exclude any mention of the 1997 American Academy of Neurology position paper. August 2010.

Louis A. Mosiello and Maria T. Mosiello v. Jocelyn O. Velenzuela, et al (case No. 02380/07), Supreme Court of the State of New York, County of Westchester, February 2011).

Richard Zawaski v. Gigs, LLC and Wendell Lee Zorman (case No. 08-2380), Commonwealth of Massachusetts. qEEG was admitted after a Daubert challenge, July 2011.

Oregon State v Glynn, Linn County No. 12112156, et al, May 13, 2013

State of Oregon v Justen Glynn - Linn County Nos 11122156, 13CR0072 & 13CR001191 Oct. 5, 2013 2013

Johnson v. Premo QEEG admitted on 12/18/13 in Post Conviction Relief matter related to a claim of Ineffective Assistance of Counsel (IAC) being heard in the Oregon State Courts. The murder occurred around 1998-1999.

State of Arkansas v. Frank Williams, Jr. July 14, 2014 QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D.)

Houston Capital Murder case, State v. Warren Rivers, Cause #047512201010-3, QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D.) October 2014.

State of Oregon v. Zane Skeen, Case No. 1300498CR. November 10, 2014. . QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D.)

Patrick Valverde v. FS 41-45 Tiemann Place LLC, Supreme Court of the State of New York, New York County, Index # 113347-08, December 2, 2014 (no Frye challenge).

State of Oregon vs Troy Douglas Adcock, Jr. (No. 1202791CR). December 11, 2014. QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D.)

State of Washington v Ezekiel Watkins, February 25, 2015. (QEEG presented after a Daubert challenge by defense expert Richard Adler, M.D.)

State of Arkansas v. Justin Anderson, Little Rock Arkansas, March 30, 2015. (QEEG presented after a Daubert challenge by defense expert Richard Adler, M.D.)

State of Washington v McEnroe Beaver, April 15, 2015 QEEG admitted. QEEG presented by defense expert forensic neuropsychologist Craig Beaver.

State of Texas v. Dominique A. Stokes, 122nd District Court of Galveston County, Texas. Case No. 11CR1157. July 17, 2015. (QEEG presented after a Daubert challenge by defense expert Richard Adler, M.D.)

State of Oregon vs David Ray Bartol (No. 14C46903). June 16, 2016. QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D.)

State of Washington v. Kenneth Jones, Case No. 14-1-05587-7-SEA. July 27, 2016. QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).

Sirvonae Stevenson v. Anthony Hedgepath Warden, Case No. /cv13-00643-0DW-JCG Central District of California, Los Angeles, November 21, 2016. QEEG admitted. (QEEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).

State of Utah v. Jayden Sterzer Third District Juvenile Court Salt Lake Division, Case No. 1042416. December 12, 2016. **QEEG admitted. (EEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).**

State of Washington v. Michael S. Thompson, Case No. 14-1-02808-0 SEA QEEG admitted March 21, 2017. (EEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).

State of Washington v. Jason Becktel, Case No. 15-1-00003-8. QEEG admitted on June 19, 2017. (EEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).

16-000324 v. Wawanesa Mutual Insurance Company – QEEG admitted to an Ontario, Canada Court that was upheld upon appeal Before: Linda P. Lamoureux, Executive Chair, For the Applicant: Parent Litigation Guardian, For the Respondent: Katherine E. Kolnhofer, May 26, 2017.

State of Idaho v. Jonathan Daniel Renfro, Case No. CR-2015-6589. QEEG admitted on October 31, 2017. (EEG analyses performed by Robert W. Thatcher, Ph.D. and Myer Proler, M.D. and presented by Richard Adler, M.D.).

People v. Andrew Urdiales, Case No.09ZF0079, County of Orange, California. QEEG admitted on April 17, 2018. (EEG analyses performed by Robert W. Thatcher, Ph.D.).