

BIOGRAPHICAL SKETCH

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NAME: Key, Alexandra Pavlovna

eRA COMMONS USER NAME (credential, e.g., agency login): keysasha

POSITION TITLE: Research Associate Professor of Hearing & Speech Sciences

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Moscow State University, Russia	BA	06/96	Psychology
Moscow State University, Russia	MA	06/97	Psychology
University of Louisville, Louisville, KY	PhD	04/02	Experimental Psychology (Cognitive)

A. Personal Statement

Dr. Key is the Director of the Psychophysiology Core and the Associate Director of the Translational Neuroimaging Core at the Vanderbilt Kennedy Center (VKC) and a member of the Vanderbilt Center for Cognitive Medicine. She has a broad background in cognitive and developmental psychology as well as psychophysiology and 20 years of research experience using cortical event-related potentials (ERPs) in studies of neurodevelopmental disorders across the life spectrum, from infancy to adulthood. In her role as the associate director of the Clinical Translational Neuroimaging Core at the VKC, she collaborates with investigators who seek to incorporate psychophysiological measures in their behavioral research programs. Dr. Key provides scientific leadership for the EEG/ERP components of such studies, including clinical trials and multisite projects (e.g., Corbett R01MH114906, Maitre R01HD081120), overseeing paradigm design, data collection, analysis, results interpretation and publication. Dr. Key’s research interests focus on psychophysiological indices of sensory and cognitive processes and their use to (a) understand mechanisms of deficits in neurodevelopmental disabilities, (b) identify markers of risk for adverse outcomes, and (c) document treatment effects. A large portion of Dr. Key’s work has been focused on the development of passive, nonverbal, IQ-independent ERP measures of cognitive and social-emotional processes suitable for use in individuals with neurodevelopmental and intellectual disabilities (e.g., autism, Angelman and Down syndromes). The findings from this line of research have validated several novel ERP findings against standardized behavioral measures and caregiver reports of adaptive functioning, and established them as sensitive markers of the effects of pharmacological and behavioral treatments aimed at improving cognitive performance and adaptive functioning.

- a) Key, A., & Yoder, P. J. (2013). Equiprobable and oddball paradigms: two approaches for documenting auditory discrimination. *Developmental Neuropsychology*, 38(6), 402–417. PMID: 23971492
- b) Key, A., & Dykens, E. M. (2014). Event-related potential index of age-related differences in memory processes in adults with Down syndrome. *Neurobiology of Aging*, 35(1), 247–253. PMCID: PMC3849808
- c) Key, A., Jones, D., Peters, S., & Dold, C. (2018). Feasibility of using auditory event-related potentials to investigate learning and memory in nonverbal individuals with Angelman syndrome. *Brain and Cognition*, 128, 73–79. PMCID: PMC6345395
- d) Key, A., & Corbett, B. A. (2019). The unfulfilled promise of the N170 as a social biomarker. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 1–12. PMID: 31679960.

B. Positions and Honors

- 1994 – 1996 Research Assistant, Moscow State University, Cognitive Processes Lab
- 1995 – 1996 Research Assistant, Slippery Rock University, Language Development Lab
- 1996 – 1997 Research Assistant, University of Louisville, Cognition and Development Lab
- 1997 – 1998 Research Associate, University of Louisville, Cognitive Neuroscience Lab, School of Medicine
- 1997 – 1999 Research Assistant, University of Louisville, Cognition and Language Lab
- 1999 – 2002 Research Assistant, University of Louisville, Developmental Neuropsychology and Electrophysiology Lab
- 1998 – 2000 Instructor, Cognitive Psychology, University of Louisville
- 2002 – 2004 Research Associate, University of Louisville, Developmental Neuropsychology and Electrophysiology Lab/Early Childhood Research Center
- 2004 – 2012 Research Assistant Professor, Department of Hearing and Speech Sciences, Vanderbilt University
- 2012 – Research Associate Professor, Department of Hearing and Speech Sciences, Vanderbilt University
- 2016 – Research Associate Professor (Adjunct), Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center
- 2004 – Director of Psychophysiology Core Services, Vanderbilt Kennedy Center for Research on Human Development, Vanderbilt University
- 2014 – Associate Director, Clinical Translational Neuroimaging Core, Vanderbilt Kennedy Center for Research on Human Development, Vanderbilt University

C. Contributions to Science

1. Established the utility of sensory event-related potential (ERP) responses for characterizing individual differences in persons with developmental disabilities.

Evaluating sensory and cognitive processes in persons with developmental disabilities can be challenging due to the limited range and low reliability of overt behavioral responses, difficulty comprehending instructions, and reduced motivation and/or attention span. Standardized behavioral assessments and caregiver- or self-reports are not always sensitive to the full range of individual differences and do not allow the direct study of neural mechanisms underlying observable performance. Dr. Key's work established that auditory and tactile ERP paradigms not requiring active responses by the participant could be successfully used across the life span and diagnostic groups to characterize quantitative differences in neurocognitive function associated with typical development, environmental influences, and atypical physiological functioning.

- a) Maitre, N., Barnett, Z., & Key, A. (2012). Novel assessment of cortical response to somatosensory stimuli in children with hemiparetic cerebral palsy. *Journal of Child Neurology*, 27(10), 1276–1283. PMID: PMC3744820
- b) Cascio, C. J., Gu, C., Schauder, K. B., Key, A. & Yoder, P. (2015). Somatosensory event-related potentials and association with tactile behavioral responsiveness patterns in children with ASD. *Brain Topography*, 28(6), 895–903. PMID: PMC4601930
- c) Peters, S., Gordon, R., & Key, A. (2015). Induced gamma oscillations differentiate familiar and novel voices in children with MECP2 duplication and Rett syndromes. *Journal of Child Neurology*, 30(2), 145–152. PMID: PMC4406405
- d) Foss-Feig, J., Stavropoulos, K., McPartland, J., Wallace, M., Stone, W., & Key, A. P. (2018). Electrophysiological response during auditory gap detection: Biomarker for sensory and communication alterations in autism spectrum disorder? *Developmental Neuropsychology*, 43(2), 109–122. PMID: PMC5972824

2. Established the utility of speech-elicited ERPs as an effective measure of communicative and language abilities in persons with/at risk for developmental disabilities.

The ability to process spoken language is critical for optimal social, emotional, and cognitive development. Through the use passive (no overt response required) ERP paradigms, Dr. Key demonstrated that ERP responses to speech stimuli (syllables and single words) can be effectively used to document multiple stages of information processing, from stimulus detection to identification and evaluation, in individuals across ages (from newborns through adults) and levels of functioning (minimally verbal to fluent). This information

supplemented available behavioral data to provide a more complete representation of communicative strengths and weaknesses and also identified potential new treatment targets.

- a) Key, A., Lambert, W., Aschner, J., & Maitre, N. (2012). Influence of gestational age and postnatal age on speech sound processing in NICU infants. *Psychophysiology*, 49(5), 720-731. PMID: PMC3324622
- b) Key, A., Yoder, P., & Stone, W. (2016). Consonant differentiation mediates a discrepancy between nonverbal and verbal abilities in children with ASD. *Journal of Intellectual Disabilities Research*, 60(5), 478-490. PMID: PMC6927012
- c) Key, A., Gustafson, S., Rentmeester, L., Hornsby, B., & Bess, F. (2017). Speech processing fatigue in children: Auditory ERP and behavioral measures. *Journal of Speech, Language, Hearing Research*, 60, 2090-2104. PMID: PMC5831094
- d) Key, A., Jones, D., & Peters, S. (2019). Spoken word processing in Rett syndrome: Evidence from event-related potentials. *International Journal of Developmental Neuroscience*, 73, 26–31. PMID: PMC6377340

3. Developed nonverbal/passive ERP paradigms to evaluate social interest and motivation in individuals with developmental disabilities.

Assessing social interest and motivation in persons with developmental disabilities can be challenging, especially in younger and nonverbal individuals, due to the common measures' significant reliance on verbal and higher-order cognitive skills. Dr. Key's research using auditory and visual ERPs demonstrated that neural responses during passive exposure to the stimuli could objectively quantify multiple levels of social information processing, from detection of and orienting to familiar vs. novel faces and voices to forming memory representations of novel social stimuli. The latter metrics are particularly informative about social stimulus salience and offer a sensitive index of individual differences in social functioning.

- a) Key, A. & Stone, W. (2012). Processing of novel and familiar faces in infants at average and high risk for autism. *Developmental Cognitive Neuroscience*. 2, 244-255. PMID: 22483074
- b) Key, A., & Corbett, B. A. (2014). ERP responses to face repetition during passive viewing: A nonverbal measure of social motivation in children with autism and typical development. *Developmental Neuropsychology*, 39(6), 474–495. PMID: PMC4142544
- c) Key, A., & Dykens, E. M. (2016). Face repetition detection and social interest: An ERP study in adults with and without Williams syndrome. *Social Neuroscience*, 11(6), 652–664. PMID: PMC5266528
- d) Key, A., & Jones, D. (2018). Social-emotional processing in nonverbal individuals with Angelman syndrome: Evidence from brain responses to known and novel names. *Journal of Intellectual Disability Research*, 63(3), 244–254. PMID: PMC6924168

4. Demonstrated the effectiveness of cortical response measures as predictors of developmental outcomes and markers of treatment effects.

Early identification of risk for poor developmental outcomes, especially prior to the emergence of behavioral symptoms, is essential to the design, implementation and maximal effectiveness of early interventions. Dr. Key's lab developed passive auditory, visual, and tactile ERP paradigms and documented their utility in infants and children with developmental disabilities as predictors and markers of cognitive, communicative, and motor outcomes. These results paved the way for using ERP as outcome measures in interventions aiming to improve adaptive functioning. The results of these studies demonstrated that ERPs are not only an effective measure of information processing at the cortical level but can inform about a broader range of processes supported by the shared neural mechanisms.

- a) Maitre, N., Lambert, W., Aschner, J., & Key, A. (2013). Cortical speech sound discrimination in the intensive care unit predicts cognitive and language development through 2 years of age. *Developmental Medicine & Child Neurology*, 55(9), 834-839. PMID: PMC3740084
- b) Yoder, P., Molfese, D., Murray, M., & Key, A. (2013). Normative topographic ERP analyses of speed of speech processing and grammar before and after grammatical treatment. *Developmental Neuropsychology*, 38(8), 514-533. PMID: PMC3873727.
- c) Matusz, P. J., Key, A., Gogliotti, S., Pearson, J., Auld, M. L., Murray, M. & Maitre, N. (2018). Somatosensory plasticity in pediatric cerebral palsy following constraint-induced movement therapy. *Neural Plasticity*, 2018(1), 1–14. PMID: PMC6250030

- d) Corbett, B. A., Ioannou, S., Key, A., Coke, C., Muscatello, R., Vandekar, S., & Muse, I. (2019). Treatment effects in social cognition and behavior following a theater-based intervention for youth with autism. *Developmental Neuropsychology*, 44, 481-494. PMID: PMC6818093

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/alexandra.key.1/bibliography/47294536/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1U54 HD083211-01A1 Neul (PI)
NIH/NICHD

09/01/2015-08/31/2020

Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center at Vanderbilt University
This grant provides core support for The Eunice Kennedy Shriver Intellectual and Developmental Disability Research Center at Vanderbilt University.

Role: Director, VKC Psychophysiology Services; Associate Director, Clinical Translational Neuroimaging Core

1R01HD081120-01A1 (Maitre)
NIH/NICHD

07/01/2015-03/31/2020

Early Childhood Constraint Therapy for Sensory/Motor Impairment in Cerebral Palsy

The goal of that randomized controlled trial to test the effectiveness of constraint-induced movement therapy combined with motor and sensory-motor interventions in children 12-24 months of age, using objective, quantitative measures to assess somatosensory, kinematic, and developmental motor function.

Role: Co-investigator & Site PI

N/A/ (Key)

07/01/2018-06/30/2020

Foundation for Angelman Syndrome Therapeutics

Biomarkers of cognition in Angelman syndrome

This project will evaluate auditory ERP and eye tracking measures of auditory learning and speech processing as a marker of cognitive functioning in persons with Angelman syndrome.

Role: PI

R01MH114906-01 (Corbett)
NIH/NIMH

12/20/2017-11/30/2021

Investigating Social Competence In Youth With Autism: A Multisite RCT

The proposed project using a multisite RCT will extend prior findings and provide a stronger test of efficacy of SENSE Theatre treatment. The overarching aim of the study is to determine whether changes in face memory and social interaction are due to the SENSE Theatre treatment and the extent to which these changes generalize and maintain.

Role: Co-Investigator

2 R01 MH102272-06 (Cascio)
NIMH

9/23/2019-7/31/2024

Bridging the Internal and External Sensory Worlds in Autism

The goal of this project is to isolate and test potential neural drivers and clinical sequelae of this disrupted integration. The proposed work will provide important new insights into the consequences of sensory processing deficits in autism that go beyond exteroceptive sensation, incorporating a sensory milieu that has high relevance for social-emotional functioning.

Completed Research Support (last 3 years)

1R21DC016144-01 (Woynaroski)
NIH/NIDCD

04/01/2017-03/31/2020

Sensory Project in Infant/Toddler Siblings of Children with Autism (Project SPIS)

This innovative and interdisciplinary project is expected to unveil links between a potentially tractable, but relatively understudied factor (early sensory responsivity) and social communication and language in infants at heightened risk for ASD.

Role: Investigator

N/A (Newhouse)

05/01/2017-06/30/2019

Alzheimer's Drug Discovery Foundation

Single Ascending Dose Phase 1 Study of Muscarinic M1PAM for Alzheimer's Disease.

The goal of this project is to propose that cholinergic stimulation of postsynaptic M₁ receptors through allosteric mechanisms (either solo treatment or together with standard AD treatment) may improve cognitive symptoms and prevent losses in cognitive abilities in AD over time, without the typical cholinergic side effects that have proved problematic with past muscarinic drug development.

Role: Investigator

1R34 DC15920-01A1 (Hood)

NIH/NIDCD

Automated Objective Audiometry using Long Latency Steady State Responses

The aim of this project is to develop an automated hearing threshold estimation system using cortical auditory long-latency evoked responses (LLR) analyzed objectively in a steady-state condition.

Role: Investigator

N/A/ (Key)

04/01/2017-08/31/2018

Foundation for Prader-Willi Research

Developing Objective Biomarkers of Hyperphagia in Children with PWS

This project will evaluate two noninvasive, low-cost measures of food-related interest using physiological processes, such as eye movements and brain activity, in 3-12-year-old children with PWS and age-matched typical children with healthy or excessive weight.

Role: PI

N/A/ (Key)

03/01/2017-02/28/2018

Foundation for Angelman Syndrome Therapeutics

Auditory brain responses as an indicator of cognitive function in Angelman syndrome

This project will evaluate feasibility of using EEG/ERP measures of auditory learning and social-emotional processing as a marker of cognitive functioning in children and adults with Angelman syndrome.

Role: PI

HeART Award #3106 Peters & Key (MPI)

10/01/2014 – 09/30/2016

International Rett Syndrome Foundation

Auditory processing, language, and learning in Rett and Rett-related disorders

The goal of this project is to develop novel, objective, auditory ERP-based measures for evaluating higher level cognitive and language functions in children with Rett and MECP2 duplication syndromes.

Role: Co-PI

VR11386 (Key)

03/25/2015-03/25/2016

Vanderbilt Institute for Clinical and Translational Research

Psychophysiological Markers of SENSE Theatre Treatment Effects in Children with ASD

The project will conduct an early stage investigation of the efficacy of a novel brain-based nonverbal measure of social stimulus salience and associated incidental memory as a marker of intervention (SENSE Theatre) effects in children with autism.

Role: PI