

BIOGRAPHICAL SKETCH

NAME: Kette Dualibi Valente

POSITION TITLE: Full Professor of Pediatric Neurology – University of São Paulo - Medicine

A. Personal Statement

My research focus on cognition, and behavioral co-existing conditions in children and young adults with epilepsy. After my PhD in Electroclinical Phenotype in Chromosomal Disorders and its Correlation with Genotype, I established the Neurodevelopmental Clinic for Epilepsy with a multidisciplinary team (Child and Adolescent Psychiatrists, Neuropsychologists, Psychologists, Sleep Disorders Group) based on the need of the patients that I was following. At the same time, as a board-certified Pediatric Neurologist with expertise in Epilepsy and Neurophysiology, I was invited as an Associated Professor to create the Clinical Neurophysiology Unit of the Psychiatry Institute, providing me a chance to interact with distinct disciplines. Interestingly, at this moment, I have the chance to combine two passions – genotype-phenotype correlation and co-existing conditions connecting the dots of my career.

I have worked as a principal investigator or co-investigator on several projects funded by the Sao Paulo Research Foundation (FAPESP) and CNPq (National Council for Scientific and Technological Development), leading to be the Co-PI in my Institution of the CINAPCE project – the most important multidisciplinary project of epilepsy of the State of São Paulo. After 10 years, I was invited to apply for a new title – Full Professor in Pediatric Neurology - which is the highest academic degree in our country and Latin America. I trained 18 fellows in neurophysiology and epilepsy, and I was the advisor in seven MSc. and five Ph.D. I was also the advisor of five undergraduate students. I am currently advising two undergraduate students, two MSc. and one Ph.D.

I am currently the consultant of Angelman Syndrome, Dravet Syndrome, CDKL5, and SYNGAP1 Foundation in Brazil. Because of this involvement, I have decided to be more active in clinical trials for these patients and I am currently the PI in four, I am also part of the board of the three most important Brazilian Pharma Industries and Local UCB in order to obtain funding for my Research Laboratory.

My current position as the Chair of the Pediatric Commission of the ILAE demonstrates my experience in administering successful projects and collaborating with researchers worldwide. It has taught me the importance of international collaboration in the context of rare disorders. As part of our research plan, Dr. Danielle Andrade and I have designed a realistic research plan that involves frequent communication among project members, timelines, and budget management. The proposed research project builds on my prior work and combines my expertise, leadership, training, and motivation to conduct the research successfully. My previous experience with research projects, regular and thematic projects, is demonstrated below.

Research Support

FAPESP 2021/14144-0 (2021-2026): Impact of High Polyunsaturated Fatty Acid Ketogenic Diet on Epileptic Seizure Control and Cognition: Correlation with Histological and Functional Aspects PI: Valente, K.

CNPq 307817/2019-9 (2019-2021): Behavioral and Cognitive Comorbidities in Epilepsy: Delineating Phenotypes across life span. PI: Valente, K.

CNPq 310850/2016-9 (2016-2018): Multimodal approach to cognitive and psychiatry comorbidities in temporal lobe epilepsy. PI: Valente, K.

FAPESP 2016/17590-3 (2016-2019): Drug-resistant epilepsies: diagnostic challenges, study of comorbidities and new experimental approaches. Role: Co-PI

CNPQ 2015: Dysfunction and degeneration of limbic circuits and its implications on the human epileptogenesis and cognitive and psychiatric disorders associated with human temporal lobe epilepsy. Role: Collaborator

FAPESP 13 / 11361-4 (10/01/2013 – 09/30/2015): Study of Association between Polymorphisms of Serotonergic Pathway and Temporal Lobe Epilepsy Caused by Hippocampal Sclerosis (TLE-HS). Role: PI

FAPESP 12/09025-3 (02/01/2012 – 02/01/2015): Executive and Mnestic Functions in Patients with Mesial Temporal Sclerosis (MTS): Association between Neuropsychological Evaluation and Novel Neuroimaging Techniques. Role: PI

CNPQ 307262/2011-1 (02/01/2012-02/01/2015): Impulsive Personality Traits and Executive Dysfunction in Patients with Juvenile Myoclonic Epilepsy and their Healthy Family Members. Role: PI.

FAPESP 05/56464-9 (04/01/ 2007 – 03/31/ 2013): Interinstitutional cooperation in support of research on the brain of the state of São Paulo. Thematic Project – Role: Co-PI

FAPESP 06/56971-0 (05/01/ 2007 – 04/30/ 2010): Personality disorder in Juvenile Myoclonic Epilepsy; Searching for possible biological bases. Role: PI

FAPESP 07/52110-3 (09/01/ 2007 – 08/31/ 2009): Juvenile Myoclonic Epilepsy (JME): The evaluation of attentional and executive functions, personality traits and social functioning. Role: PI

FAPESP 05/03489-4 (04/01/2006 – 03/31/2008): Executive function in children with temporal lobe epilepsy: correlation between neuropsychological evaluation and voxel-based morphometry (VBM). Role: PI

FAPESP 05/03527-3 (03/01/2006 – 02/28/2007): Sexual and gonadal functions in adolescents with epilepsy under monotherapy. Role :PI

FAPESP 03/07724-2 (04/01/2004 – 11/30/2006): Co-administration of lamotrigine and valproate; pharmacokinetics and pharmacodynamics interactions. Role: PI (t was the first study designed and conducted in children with epilepsy with this coadministration).

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

Positions

2000–2004	Assistant Physician – Laboratory of Clinical Neurophysiology – USP
2006	Clinical Director - Laboratory of Clinical Neurophysiology – USP
2004	Coordinator of the Group for the Study of Psychiatric Disorders and Cognitive Deficits in Epilepsy
2004	Coordinator of the Fellowship Program for Epilepsy and Clinical Neurophysiology – 18 graduated fellows
2006	Vice-Coordinator - Laboratory of Neuroimaging in Neuropsychiatric Disorders (LIM 21 – USP)
2004	Adviser of the Post-Graduation Program of the Department of Psychiatry -USP
2013	Scientific and Technical Director - Laboratory of Clinical Neurophysiology – USP

Scientific Appointments (most relevant)

2004–2008	Vice-President, Brazilian League Against Epilepsy (BLEA) – Chapter of the ILAE
2006–2008	Associate Editor (co-Founder), Journal of Clinical Neurophysiology and Epilepsy
2008	Member of the Scientific Commission of the BLAE – Pediatric Epilepsy
2004	FAPESP Peer Review Committee: Epilepsy, ad hoc reviewer
2006	CNPq Peer Review Committee: Epilepsy, ad hoc reviewer
2013 - 2017	Member - Task Force of Psychogenic Nonepileptic Seizures - Comission of Neuropsychobiology - International League Against Epilepsy
2013-2015	Member - Task Force of Psychogenic Nonepileptic Seizures, American Epilepsy Society
2018-2021	Treasurer - Commission of Psychiatry, International League Against Epilepsy
2018-2021	Member - Task Force of Psychotherapy, International League Against Epilepsy
2018-2021	Chair – Task Force of Psychiatric Issues in Pediatric Epilepsy, International League Against Epilepsy
2019-2022	Member of the Lancet Neurology Commission of the International League Against Epilepsy
2020-2022	President of the Brazilian Chapter of Epilepsy, International League Against Epilepsy
2021-2025	Member of the Research Advocacy Task Force - Pediatric Commission, International League Against Epilepsy
2021-2025	Member of the Delphi Task Force, Standard and Best Practice Council, International League Against Epilepsy
2021-2025	Chair of the Pediatric Commission of the International League Against Epilepsy
2023	Organizing and Scientific Committee of the ILAE Conference (Dublin, Ireland)
2021	Epilepsy & Behavior, Associate Editor
2020	Frontiers in Neurology, Epilepsy, Associate Editor
2020	Frontiers in Pediatric Neurology, Associate Editor
2023	Epileptic Disorder, Editorial Board
2023	EpiGraph (Digital news journal of ILAE), Editorial Board

Honors

2023	1 st in Pediatric Neurology* H Index 38 i10 Index 92 - Latin America Scientists Medical and Health Sciences / Pediatric Neurology i10 Productivity Rankings 2024
2022	Aristides Leao Award - Best Basic Science Research in Epilepsy
2013	Best Paper in Functional Neuroradiology – American Society of Neuroradiology
2012	Young Resarch Award for Ruda Alessi (post-graduate student).
2010	Cesare Lombroso Award – Best Clinical Study in Epilepsy
2010	Ten Best Studies in the Category: Epilepsy and Comorbidities. American Epilepsy Society Meeting.

C. Contributions to Science (selected publications)

Electroclinical Phenotypes and Genetics: My early publications directly addressed the electroclinical aspects of developmental encephalopathies associated with chromosomal disorders. The possibility of genotype-phenotype correlation established in Angelman syndrome determined by distinct genetic mechanism led me to the study of neurogenetics. This earlier research provided the possibility to collaborate with other forms of epilepsy.

Valente KD, Melo F, Marin R, et al. The Diagnostic Odyssey of CDKL5 Patients: A Call for Action. *Epilepsia Open* 2024 *under review*

Akula SK, Chen AY, Neil JE, et al.; Polymicrogyria Genetics Research Network. Exome Sequencing and the Identification of New Genes and Shared Mechanisms in Polymicrogyria. *JAMA Neurol.* 2023 Sep 1;80(9):980-988.

Vincentiis S, Alcantara JA, Rzezak P, et al. Genetic polymorphisms of the serotonin transporter are not related with depression in temporal lobe epilepsy caused by hippocampal sclerosis. *Epilepsy Behav.* 2021;117:107854.

Vincentiis S, Alcantara J, Rzezak P, et al. Higher transcription alleles of the MAOA-uVNTR polymorphism are associated with higher seizure frequency in temporal lobe epilepsy. *Epilepsy Res.* 2019; 149:26-29.

Alcantara JA, Vincentiis S, Santos B, et al. BDNF Val66Met polymorphism is not related with temporal lobe epilepsy caused by hippocampal sclerosis in Brazilian population. *Seizure.* 2018; 60:159-162.

Alcantara JA, Vincentiis S, Kerr DS, et al. Association study of functional polymorphisms of dopaminergic pathway in epilepsy-related factors of temporal lobe epilepsy in Brazilian population. *Eur J Neurol.* 2018; 25(6):895-901.

Alcantara JA, Vincentiis S, Kerr DS, et al. Association study of functional polymorphisms of dopaminergic pathway in epilepsy-related factors of temporal lobe epilepsy in Brazilian population. *Eur J Neurol.* 2018; 25(6):895-901.

Fonseca NC, Joaquim HP, Talib LL, Vincentiis S, Gattaz WF, Valente KD. 5-hydroxytryptamine_{1A} receptor density in the hippocampus of patients with temporal lobe epilepsy is associated with disease duration. *Eur J Neurol.* 2017;24(4):602-608.

Valente KD, Varela MC, Koiffmann CP, et al. Angelman syndrome caused by deletion: a genotype-phenotype correlation determined by breakpoint. *Epilepsy Res.* 2013; 105(1-2):234-9.

Valente KD, Koiffmann CP, Fridman C et al. Epilepsy in patients with Angelman syndrome caused by deletion of the chromosome 15q11-13. *Arch Neurol* 2006; 63(1): 122-8.

Chang BS, Apse KA, Caraballo R et al. A familial syndrome of unilateral polymicrogyria affecting the right hemisphere. *Neurology* 2006; 66(1): 133-5.

Valente KD, Fridman C, Varela MC, et al. Angelman syndrome: uniparental paternal disomy 15 determines mild epilepsy, but has no influence on EEG patterns. *Epilepsy Res.* 2005; 67(3):163-8.

Valente M, Valente KD, Sugayama SS, Kim CA. Malformation of cortical and vascular development in one family with parietal foramina determined by an ALX4 homeobox gene mutation. *AJNR Am J Neuroradiol.* 2004; 25(10):1836-9.

Valente KD, Andrade JQ, Grossmann RM, Kok F, Fridman C, Koiffmann CP, Marques-Dias MJ. Angelman syndrome: difficulties in EEG pattern recognition and possible misinterpretations. *Epilepsia* 2003; 44(8): 1051-63.

Valente KD. Another Rett patient with a typical Angelman EEG. *Epilepsia.* 2003; 44(6):873-4.

Neurodevelopmental Comorbidities and Epilepsy: As an Advisor Professor at the Neuroscience Unit, linked to the Neurology and Psychiatry Departments, with a team of collaborators and bright postgraduate students for Master and PhD Degree from neurology, psychiatry and neuropsychology, I documented comorbidities – cognitive and behavioral – in distinct types of epilepsy syndromes. This work was recognized by the International League and I was invited to be a member of the Psychiatry Commission and later on Chair of the Psychiatric Issues in Pediatric Epilepsy that was a liaison between the Psychiatry and Pediatric Commissions. In addition, most of the grants (Research Support) resulted in these manuscripts as the **senior** author.

Reilly C, et al. Jette N, Johnson EC, et al. Scoping review and expert-based consensus recommendations for assessment and management of psychogenic non-epileptic (functional) seizures (PNES) in children: A report from the Pediatric Psychiatric Issues Task Force of the International League Against Epilepsy. *Epilepsia.* 2023.

Gandy M, Modi AC, Wagner JL, et al. Managing depression and anxiety in people with epilepsy: A survey of epilepsy health professionals by the ILAE Psychology Task Force. *Epilepsia Open.* 2021;6(1):127-139.

Paiva M, Serafim A, Vincentiis S, et al. A cognitive rehabilitation program to improve hot and cool executive dysfunction in juvenile myoclonic epilepsy: Preliminary findings. *Epilepsy Behav.* 2023; 144:109281.

Koike C, Lima EM, Paiva ML, et al. Sleep quality and circadian rhythm profile of persons with juvenile myoclonic epilepsy in a tertiary epilepsy center: A case-control study. *Seizure.* 2023 Jan;104:1-5.

Oliveira MC, Lima EM, de Paiva MLN, Valente KDR. Factors associated with caregiver burden of adults with epilepsy in a middle-income country. *Seizure.* 2022 May;98:1-7.

Lima EM, Gois J, Paiva ML, et al. Anxiety symptoms are the strongest predictor of quality of life in temporal lobe epilepsy. *Seizure.* 2021; 88:78-82.

- Gandy M, Modi AC, Wagner JL, et al. Managing Depression and Anxiety in People with Epilepsy: A Survey of Epilepsy Health Professionals by The ILAE Psychology Task Force. *Epilepsia Open* 2020
- Paiva ML, Lima EM, Siqueira IB, et al. Seizure control and anxiety: Which factor plays a major role in social adjustment in patients with Juvenile Myoclonic Epilepsy? *Seizure*. 2020; 80:234-239.
- Lima EM, Rzezak P, Montenegro MA, Guerreiro MM, Valente KDR. Social cognition in childhood epilepsy with centrotemporal spikes. *Seizure*. 2020; 78:102-108.
- Paiva ML, Rzezak P, Santos B, et al. Dissociation between decision making under ambiguity and risk in patients with juvenile myoclonic epilepsy. *Epilepsy Behav*. 2019; 101(Pt A):106548.
- Auvin S, Wirrell E, Donald KA, et al. Systematic review of the screening, diagnosis, and management of ADHD in children with epilepsy. Consensus paper of the Task Force on Comorbidities of the ILAE Pediatric Commission. *Epilepsia*. 2018; 59(10):1867-1880.
- Rzezak P, Moschetta SP, Mendonça M, et al. Higher IQ in juvenile myoclonic epilepsy: Dodging cognitive obstacles and "masking" impairments. *Epilepsy Behav*. 2018; 86:124-130.
- Lima EM, Rzezak P, Dos Santos B, et al. The relevance of attention deficit hyperactivity disorder in self-limited childhood epilepsy with centrotemporal spikes. *Epilepsy Behav*. 2018 May;82:164-169.
- Lima EM, Rzezak P, Dos Santos B, et al. The relevance of attention deficit hyperactivity disorder in self-limited childhood epilepsy with centrotemporal spikes. *Epilepsy Behav*. 2018 May;82:164-169.
- Scorza FA, Scorza CA, Valente KD. Dravet syndrome, SUDEP, and omega-3 fatty acids: Lessons from the past, learning of the present, and perspectives for the future. *Epilepsy Behav*. 2017 Aug;73:286-288.
- Lima EM, Rzezak P, Guimarães CA, et al. The executive profile of children with Benign Epilepsy of Childhood with Centrotemporal Spikes and Temporal Lobe Epilepsy. *Epilepsy Behav*. 2017 Jul;72:173-177.
- Rzezak P, Lima EM, Gargaro AC, et al. Everyday memory impairment in patients with temporal lobe epilepsy caused by hippocampal sclerosis. *Epilepsy Behav*. 2017 Apr;69:31-36.
- Rzezak P, Guimarães CA, Guerreiro MM, Valente KD. The impact of intelligence on memory and executive functions of children with temporal lobe epilepsy: Methodological concerns with clinical relevance. *Eur J Paediatr Neurol*. 2017 May;21(3):500-506.
- Valente KD, Rzezak P, Moschetta SP, et al. Delineating behavioral and cognitive phenotypes in juvenile myoclonic epilepsy: Are we missing the forest for the trees. *Epilepsy Behav* 2016; 54: 95-9.
- Rzezak P, Lima EM, Pereira F, et al.. Decision-making in patients with temporal lobe epilepsy: Delay gratification ability is not impaired in patients with hippocampal sclerosis. *Epilepsy Behav*. 2016;60:158-64.
- Rzezak P, Moschetta SP, Lima E, Castro CX, Vincentiis S, Coan AC, Guerreiro AC, Busatto G, Valente KD. Distinct domains of impulsivity are impaired in juvenile myoclonic epilepsy but not in temporal lobe epilepsy. *Epilepsy Behav* 2015; 45: 44-8.
- Valente KD, Rzezak P, LaFrance WC Jr. Standard medical care for psychogenic nonepileptic seizures in Brazil. *Epilepsy Behav*. 2015 Apr;45:128-35.
- Fonseca NC, Joaquim HPG, Talib LL, et al. Hippocampal serotonin depletion is related to the presence of generalized tonic-clonic seizures, but not to psychiatric disorders in patients with temporal lobe epilepsy. *Epilepsy Research* 2015; 111: 18-25.
- Rzezak P, Valente KD, Duchowny MS. Temporal lobe epilepsy in children: executive and mnemonic impairments. *Epilepsy Behav* 2014;31: 117-22.
- Moschetta S, Valente KD. Impulsivity and seizure frequency, but not cognitive deficits, impact social adjustment in patients with juvenile myoclonic epilepsy. *Epilepsia* 2013; 54(5): 866-70.
- Guimarães CA, Rzezak P, Fuentes D, et al. Memory in children with symptomatic temporal lobe epilepsy. *Arq Neuropsiquiatr*. 2014 Mar;72(3):184-9.
- Pereira A, Valente KD. Severity of depressive symptomatology and functional impairment in children and adolescents with temporal lobe epilepsy. *Seizure*. 2013; 22(9):708-12.
- Rzezak P, Guimarães CA, Fuentes D, Guerreiro MM, Valente KD. Memory in children with temporal lobe epilepsy is at least partially explained by executive dysfunction. *Epilepsy Behav* 2012; 25(4): 577-84.
- Valente KD, Busatto Filho G. Depression and temporal lobe epilepsy represent an epiphenomenon sharing similar neural networks: clinical and brain structural evidences. *Arq Neuropsiquiatr*. 2013 Mar;71(3):183-90.
- Moschetta SP, Valente KD. Juvenile myoclonic epilepsy: the impact of clinical variables and psychiatric disorders on executive profile assessed with a comprehensive neuropsychological battery. *Epilepsy Behav* 2012; 25(4): 682-6.
- Moschetta S, Fiore LA, Fuentes D, Gois J, Valente KD. Personality traits in patients with juvenile myoclonic epilepsy. *Epilepsy Behav* 2011; 21(4): 473-7.
- Gattaz WF, Valente KD, Raposo NR, Vincentiis S, Talib LL. Increased PLA2 activity in the hippocampus of patients with temporal lobe epilepsy and psychosis. *J Psychiatr Res*. 2011; 45 (12): 1617-20.

Biosketch: Kette D. Valente

Rzezak P, Guimarães C, Fuentes D, Guerreiro MM, Valente KD. Episodic and semantic memory in children with mesial temporal sclerosis. *Epilepsy Behav* 2011; 21(3): 242-7.

Gois J, Valente KD, Vicentiis S, Moschetta S, Kuczynski E, Fiore L, Fuentes D. Assessment of psychosocial adjustment in patients with temporal lobe epilepsy using a standard measure. *Epilepsy Behav* 2011; 20(1):89-94.

Rzezak P, Fuentes D, Guimarães CA, Thome-Souza S, Kuczynski E, Guerreiro M, Valente KD. Executive dysfunction in children and adolescents with temporal lobe epilepsy: is the Wisconsin Card Sorting Test enough? *Epilepsy Behav* 2009; 15(3): 376-81.

de Vincentiis S, Febrônio MV, da Silva CA, Saito MI, Takiuti AD, Valente KD. Sexuality in teenagers with epilepsy. *Epilepsy Behav*. 2008 Nov;13(4):703-6.

Thome-Souza MS, Kuczynski E, Valente KD. Sertraline and fluoxetine: safe treatments for children and adolescents with epilepsy and depression. *Epilepsy Behav* 2007; 10(3):417-25.

Rzezak P, Fuentes D, Guimarães CA, Thome-Souza S, Kuczynski E, Li LM, Franzon RC, Leite CC, Guerreiro M, Valente KD. Frontal lobe dysfunction in children with temporal lobe epilepsy. *Pediatr Neurol* 2007; 37(3): 176-85.

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<https://www.ncbi.nlm.nih.gov/myncbi/kette.valente.1/bibliography/public/>

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