## BIOGRAPHICAL SKETCH

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NAME: Dapretto, Mirella

eRA COMMONS USER NAME (credential, e.g., agency login): DAPRETTO2

POSITION TITLE: Professor

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 |
|---|---|---|---|
| University of California, Los Angeles | B.A. | 08/1988 | Psychology |
| University of California, Los Angeles | M.A. | 01/1991 | Developmental Psychology |
| University of California, Los Angeles | Ph.D. | 08/1994 | Developmental Psychology |
| University of California, Los Angeles | Postdoctoral | 06/1999 | Neuroimaging |

### A. Personal Statement

After receiving a Ph.D. in Developmental Psychology with a minor in Behavioral Neuroscience, I acquired expertise in neuroimaging methods as a postdoctoral fellow at the UCLA Ahmanson-Lovelace Brain Mapping Center. Since joining the faculty of the UCLA Semel Institute for Neuroscience and Human Behavior in 1999, I have been the recipient of NIH funding to study the neural networks suberving language functions in neurotypical individuals as well as several awards to study the neural basis of the core deficits observed in autism. In 2007-2012, I served as the PI of the imaging project (Project 3) of the first NIH-funded UCLA Autism Center of Excellence (ACE). As part of our renewed ACE (2012-2017), I continue to serve as the PI of the imaging project (Project 4), and I am also the Co-PI of a project in infants at ultra high-risk for autism (Project 1). My current research is also funded though an ongoing NIH-funded multi-site (Yale, UCLA, Harvard, University of Washington) ACE Network on which I serve as Co-PI for the UCLA site, and by a recent NIH-funded multisite consortium on neurodevelopmental and behavioral predictors and consequences of substance abuse in children and adolescents. Lastly, I am also Co-PI on another NIH-funded multisite project – the Lifespan Human Connectome: Development (HCP-D) – which aims to characterize the development of functional brain networks and brain-behavior relationships from childhood to young adulthood. Relevant to my training experience, in 2010-2012 I also served as the Director of the UCLA Center for Culture, Brain, and Development, a center whose graduate training program aimed to raise a new generation of scientists who are well versed in the methods of different disciplines. Based on these experiences, my dual training as a developmental psychologist and a neuroscientist, my strong background in pediatric neuroimaging – including some of the very first longitudinal investigations using fMRI, and my past and ongoing research interest in combining imaging, genetic, and behavioral data to better characterize both typical and atypical brain development, I am extremely well positioned to oversee the successful implementation of the research proposed in Project 1 and 3 of our ACE. Some examples of influential work which resulted from ongoing collaborations supported by the UCLA ACE are listed below.

Hernandez LH, Krasileva K, Green SA, Sherman LE, Ponting C, McCarron R, Lowe JK, **Geschwind** DH, **Bookheimer** SY, & **Dapretto** M (In Press) Additive Effects of Oxytocin Receptor Gene Polymorphisms on Reward Circuitry in Youth with Autism. Molecular Psychiatry.

Green SA, Hernandez LA, **Bookheimer** SY, **Dapretto** M 2016 Salience Network Connectivity in Autism Is Related to Brain and Behavioral Markers of Sensory Over-responsivity. J Am Acad Child Adolesc Psychiatry, 55, 618-626. PMID: 27343889 - PMCID: PMC4924541

Green SA, Hernandez LA, Tottenham N, Krasileva K, **Bookheimer** SY, **Dapretto** M 2015 The Neurobiology of Over-Responsivity in Youth with Autism Spectrum Disorders. JAMA Psychiatry, 72, 778-86. PMID: 26061819 – PMCID: PMC4861140

Rudie JD, Hernandez LH, Colich NL, Gorrindo P, **Bookheimer** SY, **Geschwind** DH, Levitt P, & **Dapretto** M 2012 Autism-Associated Promoter Variant in *MET* Impacts Functional and Structural Brain Networks. Neuron, 75, 904-15. PMID: 22958829 - PMCID: PMC3454529

### B. Positions and Honors

**Positions and Employment**

| | |
|---|---|
| 1990 - 1994 | Teaching Fellow, Dept. of Psychology, UCLA |
| 1990 - 1994 | Graduate Researcher, Dept. of Psychology, UCLA |
| 1994 - 1999 | Post Doctoral Fellow, Dept. of Psychiatry and Biobehavioral Sciences, UCLA |
| 1999 - 2006 | Assistant Professor, Dept. of Psychiatric and Biobehavioral Sciences, UCLA |
| 2006 - 2012 | Associate Professor, Dept. of Psychiatric and Biobehavioral Sciences, UCLA |
| 2010 - 2012 | Director, Center for Culture, Brain, and Development, UCLA |
| 2012 - present | Professor, Dept. of Psychiatric and Biobehavioral Sciences, UCLA |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 1998 - 2000 | Editorial Board, Developmental Psychology |
| 2007 - present | Editorial Board, Autism Research |
| 2011 - present | Editorial Board, Brain and Behavior |
| Member | Society for Neuroscience, Organization for Human Brain Mapping, Cognitive Neuroscience Society, International Society for Autism Research, UCLA Brain Research Institute, UCLA Center for Culture, Brain, and Development |

**Honors and Awards**

| | |
|---|---|
| 1993 - 1994 | Dissertation Research Award, Dept. of Psychology, UCLA |
| 1995 - 1999 | Brain Mapping Post-Doctoral Fellowship, Dept. of Psychiatry, UCLA |
| 2001 - 2004 | Cure Autism Now Young Investigator Award |
| 2003 - 2006 | National Alliance for Autism Research Award |
| 2007 - 2009 | Cure Autism Now Pilot Research Award |
| 2007 - 2010 | Autism Speaks Basic Research Award |

### C. Contributions to Science

1. In my early neuroimaging research, I pioneered the use of fMRI activation paradigms which rely on selective attention mechanisms to identify the neural underpinnings of distinct linguistic functions. The first study in this series unequivocally demonstrated a dissociation for different aspects of sentence processing (syntax vs. semantics) within left frontal language areas. Importantly, these activation paradigms are particularly well suited to be used with children of different ages and developmental levels, as potential confounds due to the use of different cognitive strategies across age groups or clinical populations are greatly minimized. Using a series of innovative and ecologically valid paradigms, my research in this area has characterized the neural networks subserving different linguistic and socio-communicative functions in children with autism spectrum disorders (ASD) and typically-developing controls, as well as in the neurotypical adult brain (including the bilingual brain) as studies on adults provide a normative developmental endpoint for our developmental investigations and also allow us to address issues of brain plasticity.

a. **Dapretto M** & Bookheimer SY 1999 Form and Content: Dissociating Syntax and Semantics in Sentence Comprehension, Neuron, 24:427-432. PMID: 10571235

b. Wang AT, Lee SS, Sigman M, & **Dapretto** M 2006 Neural Basis of Irony Comprehension in Children with Autism: The Role of Prosody and Context. Brain, 129, 932-943. PMID: 16481375 - PMCID: PMC3713234

c. Wang, AT, Lee, SS, Sigman, M, & **Dapretto** M 2007 Reading Communicative Intent in the Face and Voice: An fMRI Study in Children with Autism Spectrum Disorder. Archives of General Psychiatry, 64, 698-708. PMID: 17548751 - PMCID: PMC3713233

d. Hubbard AL, Wilson SM, Callan DE, & **Dapretto** M 2009 Giving Speech a Hand: Gestures Modulates Activity Auditory Cortex Activity during Speech Perception. Human Brain Mapping, 30, 1028-37. PMID: 18412134 - PMCID: PMC2644740

2. Despite a vast literature on the neural correlates of language, very few studies have focused on the neural mechanisms underlying language *learning* and most did so in ways that bear no resemblance to the process of learning a new language in real life. Word segmentation – the detection of word boundaries in continuous speech – is a critical first step during early language learning (contrary to popular belief, there are no pauses between words) and milestone behavioral studies in infants showed that a novel speech stream can be readily segmented based on the statistical (i.e., transitional probabilities) and speech cues (i.e., stress) afforded by the input. With my graduate students, we adapted the paradigm used in prior infant research to examine how the brain accomplishes this computational feat using fMRI and investigated how the brain 'cracks' the code of a new language in the adult brain (a), developmental changes in the neural architecture subserving language learning (b,d), and altered learning-related neural activity in youth with ASD (c). By focusing on the neural mechanisms underlying language learning – as these occur online – this line of research may ultimately help answer the long-standing question of why children are better language learners than adults, as well as identify altered developmental trajectories in children with delayed and/or disordered language acquisition.

a. McNealy K, Mazziotta JC, & **Dapretto** M 2006 Cracking the Language Code: Neural Mechanisms Underlying Speech Parsing. Journal of Neuroscience, 26, 7629-39. PMID: 16855090 - PMCID: PMC3713232

b. McNealy K, Mazziotta JC, & **Dapretto**, M 2010 The Neural Basis of Speech parsing in Children and Adults. Developmental Science, 13, 385-406.

c. Scott-Van Zeeland AA, McNealy K, Wang t, Sigman M, Bookheimer S, **Dapretto M** 2010 No Neural Evidence of Statistical Learning during Exposure to Artificial Language in Children with ASD. Biological Psychiatry, 68, 345-351.

d. McNealy K, Mazziotta JC, & **Dapretto** M 2011 Age and Experience Shape Developmental Changes in the Neural Basis of Language Learning. Developmental Science, 14, 1261-1282. PMID: 22010887 - PMCID: PMC3717169

3. Over the past decade, a large component of my research has focused on characterizing the neural basis of core deficits in ASD. With several graduate students in my lab, I conducted many influential fMRI studies in children with ASD which, amongst others, refuted simple 'lesion-deficit' models of ASD while highlighting deficits in social attention (a), linked dysfunction in the putative 'mirror neuron system' to the social impairments observed in ASD (b), demonstrated reward circuitry hyporesponsivity to social stimuli thus providing support for the Social Motivation Theory of ASD (c), and showed for the first time that sensory over-responsivity in ASD is associated with sensory-limbic hyperactivation to mildly aversive stimuli (particularly when multiple modalities are presented simultaneously) and, importantly, that this hyper-responsivity is due to failure to habituate (d). Additional studies identified alterations in the neural networks subserving the processing of directed vs. averted gaze, gestures accompanying speech, self-other representations, and social orienting.

a. Wang AT, Lee SS, Sigman M, & **Dapretto** M 2007 Reading Communicative Intent in the Face and Voice: An fMRI Study in Children with Autism Spectrum Disorder. Archives of General Psychiatry, *64,* 698-708. PMID:17548751 - PMCID: PMC3713233

b. **Dapretto** M, Davies M, Pfeifer JH, Scott A, Sigman M, Bookheimer SY, & Iacoboni M 2006 Understanding Emotions in Others: fMRI Evidence of Mirror Neuron Dysfunction in Children with Autism Spectrum Disorders. Nature Neuroscience, 9, 28-30. PMID: 16327784 - PMCID: PMC3713227

c. Scott-Van Zeeland, AA, **Dapretto**, M, Ghahremani, DG, Poldrack, RA, Bookheimer, SY 2010. Reward Processing in Autism. Autism Research, 3, 53-67. PMID: 20437601 - PMCID: PMC3076289

d. Green SA, Rudie JD, Colich NL, Wood JJ, Shirinyan D, Hernandez L, Tottenham N, **Dapretto** M, Bookheimer SY 2013 J Am Acad Child Adolesc Psychiatry, 52:1158-72. PMID: 24157390 - PMCID: PMC3820504

4. In addition to my work on ASD, a considerable portion of my research is devoted to the study of typical brain development with a particular focus on a developmental period – the transition from childhood into adolescence – that heralds a time of heightened vulnerability when natural tendencies to explore and take

risks, combined with the increased influence of peers, leads to a sharp increase in dangerous behaviors as well as the onset of psychopathology. As part of this effort, with one of my graduate students, we conducted a series of studies which focused on the neural correlates of social exclusion (a) showing, among others, that heightened subgenual anterior cingulate responses to peer rejection during early adolescence predict increased risk for later depression (b). Other significant contributions to this field include some of the first longitudinal fMRI studies that examined the link between emotional reactivity and resistance to peer pressure/risk taking behavior during the transition into adolescence (c), and the neural basis of self-concept development (d). These findings have important implications because early theorizing in this area typically involved relatively simplistic models of how cognitive and affective systems change across this period of development rather than considering with greater specificity the coordination of social, cognitive, and affective systems working together in increasingly mature ways to regulate emotion and behavior during adolescence.

a. Masten CL, Eisenberger NI, Borofsky L, Pfeifer JH, McNealy K, Mazziotta JC, & **Dapretto** M 2009 Neural Correlates of Social Exclusion during Adolescence: Understanding the Distress of Peer Rejection. Soc Cogn Affect Neurosci, 4*, 143*-157. PMCID: PMC2686232

b. Masten CL, Eisenberger NI, Borofsky LA, McNealy K, Pfeifer JH, & **Dapretto** M 2011 Subgenual Anterior Cingulate Responses to Peer Rejection: A Marker of Adolescents' Risk for Depression. Development and Psychopathology, 23, 283-292. PMCID: PMC3229829

c. Pfeifer JH, Masten CL, Moore WE, Oswald TM, Mazziotta JC, Iacoboni M, & **Dapretto** M 2011 Entering Adolescence: Resistance to Peer Influence, Risky Behavior, and Neural Changes in Emotion Reactivity. Neuron, 69, 1029-36. PMID: 21382560 - PMCID: PMC3840168

d. Pfeifer JH, Kahn LE, Merchant, JS, Peake SA, Veroude K, Masten CL, Lieberman MD, Mazziotta JC, & **Dapretto** M 2013 Longitudinal change in the neural bases of adolescent social self-evaluations: Effects of age and pubertal development. Journal of Neuroscience, 33, 7425-9. PMID: 23616547 - PMCID: PMC3809090

5. In recent years, it has become increasingly evident that a better understanding of both typical and atypical brain development can only be achieved by using a multimodal approach whereby brain-based measures are combined with genetic and behavioral data to begin to characterize complex gene-brain-behavior relationships. Accordingly, my research in both typically-developing children and children with ASD now involves acquiring task-related fMRI (a,c), resting-state fMRI (b), structural MRI (b), and ASL perfusion (d) data as well as extensive phenotyping and genotyping (c) all *within* the same individuals in order to chart both normative and altered brain function, structure, and connectivity. Importantly, some of our recent imaging genetic findings (see references following the Personal Statement) have highlighted how genetic stratification may reduce heterogeneity thus helping elucidate the biological basis of complex neuropsychiatric disorders such as ASD.

a. Rudie JD, Shehzad Z, Hernandez L, Colich NL, Bookheimer SY, Iacobomi M, & **Dapretto** M 2012 Reduced Functional Integration and Segregation of Distributed Neural Systems Underlying Social and Emotional Information Processing in Autism Spectrum Disorders. Cerebral Cortex, 22, 1025-37. PMID: 21784971 - PMCID: PMC3328339

b. Rudie JD, Shezad Z, Hernandez LH, Colich NL, Bookheimer SY, & **Dapretto** M 2013 Altered Functional and Structural Brain Network Organization in Autism. NeuroImage: Clinical, 2, 79-94. PMID: 24179761 - PMCID: PMC377770811.

c. Scott-Van Zeeland AA, Abrahams BS, Alvarez-Retuerto AI, Sonnenblick LI, Rudie J, Ghahremani D, Mumford J, Poldrack RA, **Dapretto** M, Geschwind DH, & **Bookheimer** SY 2010 Altered Functional Connectivity Associated with Variation in CNTNAP2. Science Translational Medicine, 2:56ra80. PMID: 21048216 - PMCID: PMC3065863

d. Jann K, Hernandez LM, Beck-Pancer D, McCarron R, Smith RX, **Dapretto** M, Wang DJ. 2015 Altered resting perfusion and functional connectivity of default mode network in youth with autism spectrum disorder. Brain Behav, 5(9):e00358. PMID:26445698 - PMCID:PMC4589806

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/mirella.dapretto.1/bibliography/41271471/public/?sort=date&direction=descending

**D. Research Support**

**Ongoing Research Support**

NICHD P50 HD055784 (Center PI: Bookheimer) 08/01/12-05/31/17
Autism Center of Excellence Project 4
*Neuroimaging Signatures of Autism: Linking Brain Function to Genes and Behavior*
This project will chart longitudinal changes in brain activity and connectivity in children with and without ASD, and to relate the observed developmental trajectories to both behavioral phenotypes and autism risk genes.
Role: PI (Project 4)

NICHD P50 HD055784 (Center PI: Bookheimer) 08/01/12-05/31/17
Autism Center of Excellence Project 1 (PI: Jeste)
*Neural Assays and Longitudinal Assessment of Infants at Very High Risk for ASD*
This project aims to identify reliable biological markers of autism in infants at ultra-high for the disorder using eye tracking, pupillometry, electrophysiology, and magnetic resonance imaging.
Role: Co-PI (Project 1)

NIMH RO1 MH100028 (Center PI: Pelphrey) 08/01/12-07/31/17
UCLA Site PI: Bookheimer
*Multimodal Developmental Neurogenetics of Females with ASD*
This multi-site project examines sex differences in brain structure, function, connectivity, and temporal dynamics and relate these differences to heterogeneity in ASD behavior and genetics.
Role: Co-PI UCLA Site

NICHD R01 HD079432 (USC PI: Aziz-Zadeh) 04/01/15-01/31/20
UCLA Subcontract (PI: Dapretto)
*The neural basis of motor, social and emotional deficits in children with ASD*
These studies will qualify the neural underpinnings of core autism deficits focusing on circuits underlying shared representations.
Role: Site PI

345389 Simons Foundation Autism Research Initiative (PI: Bookheimer) 09/01/15-08/31/17
*Parameterizing Neural Habituation in ASD with Sensory Over-responsivity*
The proposed study will examine brain activity and physiological responses (galvanic skin response, heart rate) in children with ASD with/without sensory over-responsivity (SOR).
Role: Co-Investigator

NIDA U01 DA041048 (PI: Sowell) 10/01/15-09/30/20
UCLA subcontract (PI: Bookheimer)
*8/13 ABCD-USA Consortium: Research Project*
This longitudinal study aims to prospectively determine the neurodevelopmental and behavioral predictors and consequences of substance abuse in children and adolescents.
Role: Site Co- PI

NIMH 1U01MH109589-01 (Van Essen) 03/01/16-02/28/20
UCLA Site (Site PIs: Bookheiner, Dapretto)
*Mapping the Human Connectome During Typical Development*
This project will use structural and functional imaging methods to characterize human brain circuitry in a large population of children and adolescents, from ages 5 to 21.
Role: Site Co- PI

**Completed Research Support**

NIMH R01 MH080892 (PI: Wang) 04/15/09-02/15/14
*Pediatric Template of Brain Perfusion*
The goal of this project is to develop a functional template or atlas of the normal pediatric brain using arterial spin labeling perfusion MRI.
Role: Co-Investigator