Sensory Processing From Bedside to Brain Training

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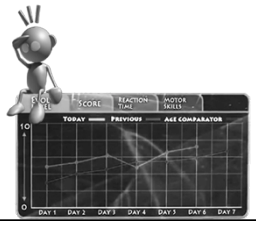
Director, PBC Sensory Neurodevelopment & Autism Program (SNAP)

Disclaimers/Conflicts

- Akili Interactive Labs: I provide consultation for the development of cognitive training tools for children.



The hour's Objectives:

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1) Understand what is meant by the term "Sensory Processing Disorder (SPD)"
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4) To understand the similarities and differences in brain connectivity between SPD and Autism
5) Understand the role of brain training in SPD and cognitive disorders

What's the big deal, anyway?

- Three Stories show the many faces of SPD:
  - Touchy Tommie
  - Fragile Frankie
  - Happy Heidi

Touchy Tommy

- y.o. male could only wear one pair of shorts.
  - Tactile: At intake in August of 2015 had one and only one pair of shorts and shirt that he had worn daily for the past year
  - Auditory: Bothered by Loud and Novel noises
  - Receiving OT support for fine motor dysgraphia
  - Frequent Meltdowns at home but not school
  - Distractible but not significantly interfering with learning
- Birth, Medical, Surgical and/or Family history is notable for meatal stenosis repair and nasal turbinate repair, mom with mild tactile sensitivity
- Activities include: trouble with bike, swimming/trampoline
- Therapies include: OT
- Medications: To be determined

Fragile Frankie

- y.o. male with a neurodevelopmental disorder characterized by
  - Strengths in gross motor (zip line, climbing)
  - challenges with fine motor (ADLs and handwriting), rec/expressive language (est 3-4y); social limited by language and arousal, attention (working on this with teachers), Sensory OverResponsivity auditory and tactile.
- Birth, Medical, Surgical and/or Family history is notable for twin delivery, overseas adoption, early neglect, ear tubes
- Comorbid conditions include: none
- Examination is notable for hypertelorism, course facial feature- triangular face, short stature
- Etiologic evaluations at referral included: psychology label of autism, no genetic evaluation
- Activities include: hippotherapy, swimming and paddle boarding
- Therapies include: ST/OT/ABA

Happy Heidi

- y.o. female with a neurodevelopmental disorder characterized by
  -
  - speed, feeling anxiety, Sensory OverResponsivity auditory only; social finesse
- Examination is notable for immature affect, non-dysmorphic and non-focal
- Etiologic evaluations to date include: Clinical MRI showed no evidence of abnormality, high resolution chromosomes, fragile X and Array were normal. Whole Exome Sequencing was revealing.
- Activities include: horse back riding, martial arts
- Current Therapies include: social skills group

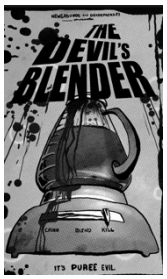
So do they have SPD?

A description? A label? or A diagnosis?

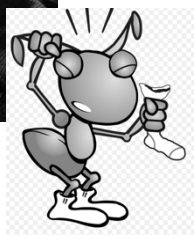
What is SPD?

- **Neuroscience/Neurologists (BROAD)**
  - The disruption of information perception, encoding, integration from one or multiple sensory systems leading to clinically relevant cognitive and behavioral deficits.
- **Occupational Therapy (SPECIFIC)**
  - A singular condition that exists when sensory signals don't get organized into appropriate responses (SPDfoundation.net)
- **Psychology/Psychiatry (NON-EXISTANT)**
  - A disorder that doesn't exist (not included in the DSM 5) but now included in Autism Spectrum Disorders Criteria
- **Pediatricians (TAG ALONG)**
  - When sensory problems are present, health care providers should consider other developmental disorders, including autism spectrum disorders, attention deficit/hyperactivity disorder, developmental coordination disorder and anxiety disorder (www.aap.org)

Auditory OverResponsive (AOR)

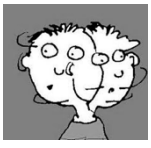


Tactile OverResponsive (TOR)



The Add On's

- Dysgraphia (fine motor control)
- Emotional Dysregulation (emotional Control)
- Inattention (Cognitive Control)



In the word of Rachel Schneider

What's it like to have SPD - SMD? It depends on the SPDer's individual experiences and specific subtype.

"For example, the sight of light may be perceived as painful, problematic, and supremely bright for those who are **over-responsive**. A person who is **sensory-seeking** might crave light and turn on every lamp in the house. Someone who is **under-responsive** might not even notice light and leave lamps on, even as they sleep…"

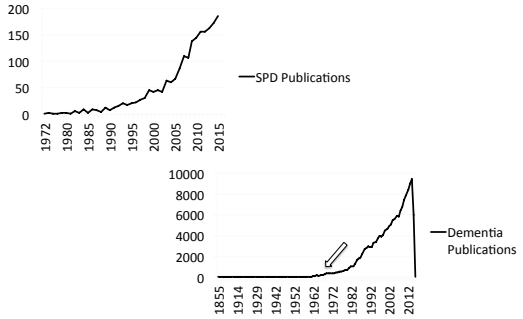
www.rachel-schneider.com

SPD Subtypes

-
  -
  - Sensory Overresponsivity: Avoiding Sensory input
  - Underresponsive: non-responsive to sensory input
-
  - Dyspraxia/Motor Planning
  - Postural Control Disorders
-

Lucy Miller: Spdfoundation.org

Whatever it is, research is on the rise…



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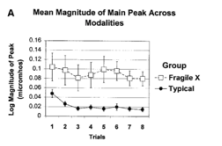
Etiologies of SPD

-
- *Utero*
-
- ?

Genetic disorders with reported SPD

-
  - Turner's (XO) and 47,XXX
- (included Triplet Repeats)
  - 16p11.2 Deletions and Duplications
  - Fragile X



Am J Med Genet. 1999 Apr 2;83(4):268-79.

[American journal of medical genetics] **sensory stimuli in individuals with fragile X syndrome: a preliminary report.**

Miller LJ, McIntosh DN, McGrath J, Shyu V, Lampe M, Taylor AK, Tassone F, Neitzel K, Stackhouse T, Hagerman RJ.

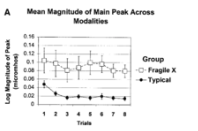
Fragile Frankie

Fragile X PCR

SEE DELAFF

RESULT: MALE, 600 CGG REPEATS (FULL MUTATION, AFFECTED)

Interpretation: The status of the Fragile X locus (FMR1) was determined by PCR amplification and Southern blot analysis, using DNA isolated from a blood specimen. This male individual is positive for a hypermethylated FMR1 allele in the full mutation size range with approximately 600 CGG repeats. Therefore, this individual is predicted to be affected by Fragile X syndrome. Family studies and genetic counseling are recommended. Laboratory results and submitted clinical information reviewed by Neng Chen, Ph.D., DABMG, CGMBS.



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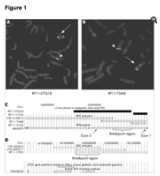
Single Genes Associated with SPD

ArhGEF9 (Rho Guanine Nucleotide Exchange Factor 9)

-
- collybistin
- Molecular switch that is pivotal in the role of post synaptic glycine and GABA receptor clusters
- Global NDD and auditory hypersensitivity (startle)



BMJ Case Rep. 2009;2009. pii: bcr06.2009.1999. doi: 10.1136/bcr.06.2009.1999. Epub 2009 Jul 2.

ARHGEF9 disruption in a female patient is associated with X linked mental retardation and sensory hyperarousal.

Marco EJ[1], Abidi FE, Bristow J, Dean WB, Cotter P, Jeremy RJ, Schwartz CE, Sherr EH.

Happy Heidi

MBD5 (methyl-CpG-Binding Domain Protein 5)

- 2q23.1
- de novo mutation in a pilot series of 10 trios with SPD
- Found in 0.18% of patients with ASD, no controls
- Cognitive Impairment, epilepsy, sleep and & behavioral challenges (3 case reports)
- Our patient:
  - WISC VCI 106, PRI 79, WMI 99, PSI 65
  - Social Communication Questionnaire total = 7
  - Sensory Profile DD in all categories
  - Vanderbilt Parent: meets ADHD cut scores
  - Clinical MRI unrevealing

Injury/Brain malformation can lead to "sensory processing differences"

- Fetal Alcohol Syndrome
- **Prematurity**
- Stroke
- Infection
- **Agenesis of the corpus callosum**
- ?Migraine?

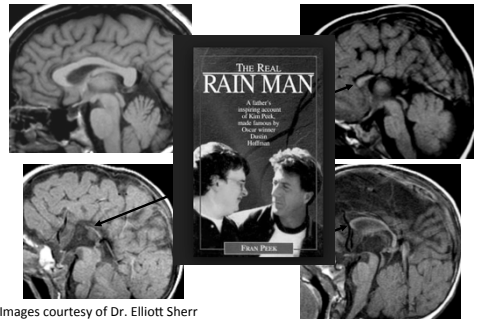
Prematurity

Atypical Sensory Behavior in Premature Infants using the Sensory Profile

	N	% with scores >2 SD* from the mean	p-value
QUADRANTS			
Low Registration	91	24	<0.01
Sensory Seeking	85	11	0.02
Sensory Sensitivity	90	10	0.03
Sensory Avoiding	87	11	0.01
SECTIONS			
Auditory Processing	99	12	<0.01
Visual Processing	96	2	0.19
Tactile Processing	86	10	0.02
Vestibular Processing	102	13	<0.01
Oral Sensory Processing	88	9	0.08

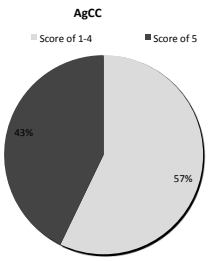
Children born prematurely have atypical sensory profiles.
Wickremasinghe AC, Rogers EE, Johnson BC, Shen A, Barkovich AJ, Marco EJ.
J Perinatol. 2013 Aug;33(8):631-5.

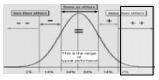
Agenesis of the Corpus Callosum



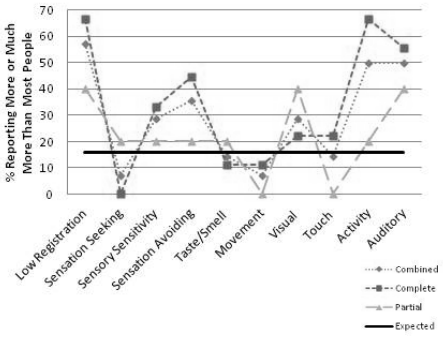
Images courtesy of Dr. Elliott Sherr

Agenesis of the Corpus Callosum: Low Registration



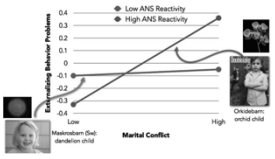


Individuals with agenesis of the corpus callosum show sensory processing differences as measured by the sensory profile.
Demopoulos C, Arroyo MS, Dunn W, Strominger Z, Sherr EH, Marco E.
Neuropsychology. 2015 Sep;29(5):751-8.



Environment (Experience over Time)

- Sensory Deprivation v. Engagement/Experience
- Trauma/Conflict v. Comfort
- Screen Time: passive v. active, addictive v. stimulating



The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: the role of laboratory stressors.
Obradović J, Bush NR, Boyce WT.
Dev Psychopathol. 2011 Feb;23(1):101-14

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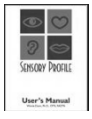
So how does one define SPD for research?

Isolated SPD



Our Lab approach (it's a start)

- Community diagnosis/suspicion of "SPD"
- Sensory Profile with > 2 SD (Definite Difference) bias toward hypersensitivity
  - Auditory, Tactile, Visual, Oral/Olfactory, Vestibular, Multisensory Processing
- Evaluate for Autism Criteria
- Evaluate for Cognitive Ability
- Evaluate for Attention/Hyperactivity
- R/o for Clinical MRI findings
- R/o for known Genetic conditions
- (Future: Assess for Dyslexia and Autonomic Arousal)…

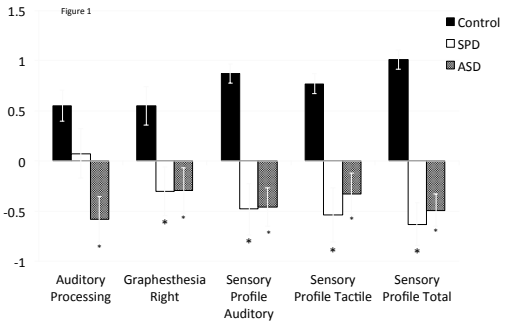
Bedside

Shared and Divergent Auditory and Tactile Processing in Children with Autism and Children with Sensory Processing Dysfunction Relative to Typically Developing Peers.
Demopoulos C, Brandes-Aitken AN, Desai SS, Hill SS, Antovich AD, Harris J, Marco EJ.
J Int Neuropsychol Soc. 2015 Jul 6:1-1

Auditory and Tactile Assessment

- 54 boys (ASD 20, SPD 15, TDC 19)
- Auditory processing: Differential Screening test for Processing (DSTP)
  - Dichotic listening (number to both ears)
  - Temporal Patterning (order of high/low tones)
  - Auditory Discrimination (Filtering-nonsense in noise)
- Tactile Processing
  - Tactile detection "Von Frey Hairs"
  - Sensitivity "two point discriminator"
  - Form Discrimination "von boven domes"
  - Proprioception/WM "SIPT graphesthesia"

Parent report & Direct Assessment

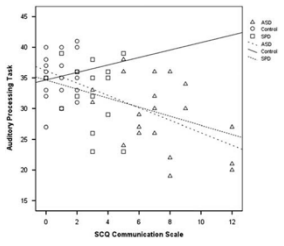


Tactile

- Tactile detection
  - Weaker detection in SPD group than ASD or TDC
- Sensitivity
  - No difference noted
- Form Discrimination "von boven domes"
  - No differences noted
- Proprioception/WM "SIPT graphesthesia"
  - Right Hand: ASD = SPD < TDC

Auditory

- ASD < SPD = TDC



r=-.34, p=.045)

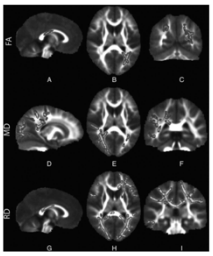
Bedside Summary

- Measurable bedside tactile differences in children with isolated SPD
- Auditory processing differences become apparent when moving to a correlational approach

But where is it in the brain ?

Structural Neuroimaging in SPD

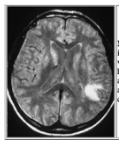
- TBSS Data Driven Approach SPD boys 8-12y compared to Controls



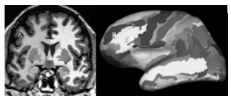
- Right handed boys
  - SPD n=16
  - Controls n=25
- Age Matched
  - 8 to 11 years old
- FSIQ matched
  - SPD mean 113 (100-131)
  - Control mean 115 (97-130)

Then, we looked for lesions…

Group	SPD (n=16)	Controls (n=25)
Corpus Callosum	0	0
Decreased White matter	0	0
Grey Matter Injury	0	0
Posterior Fossa Cyst	0	0



Next, we looked for volume…



Free Surfer		p
	Total Cortex	.87
	Intracranial	.63
	Total White	.49
	Left White	.58
	Right White	.42
	Left Cortex	.94
	Right Cortex	.81

Finally, we looked at white matter integrity using diffusion tensor imaging

+

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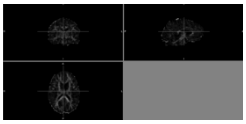
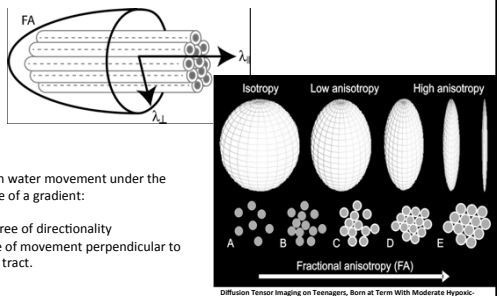


Fractional Anisotropy & Radial Diffusivity



Based on water movement under the influence of a gradient:

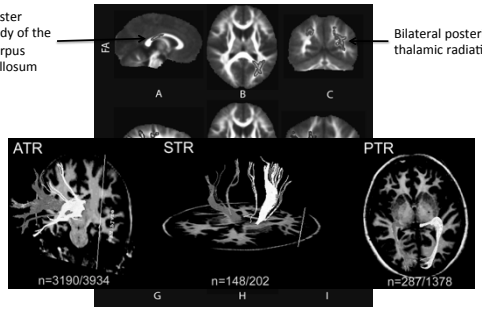
FA= Degree of directionality
RD= rate of movement perpendicular to the WM tract.

Diffusion Tensor Imaging on Teenagers, Born at Term With Moderate Hypoxic-Ischemic Encephalopathy Zoltan Nagy, Katarina Lindström, Helena Westerberg, Stefan Skare, Jesper Andersson, Boubou Hallberg, Anders Lilja, Olof Flodmark, Hugo Lagercrantz, Torkel Klingberg and Elisabeth Fernell

The differences were striking!

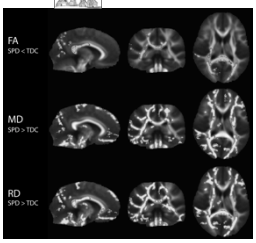
Poster Body of the Corpus Callosum

Bilateral posterior thalamic radiations



http://brain.oxfordjournals.org/content/128/11/2562/F7.large.jpg

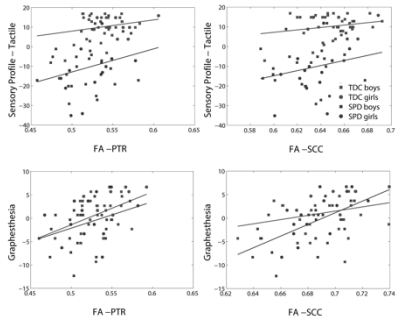
Follow up Study



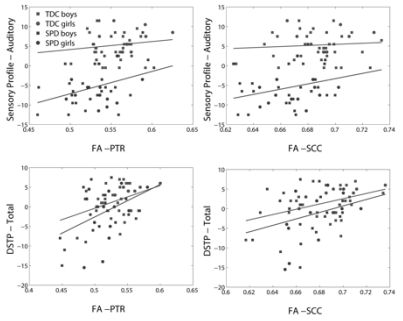
- SPD n=41 (m 28, f 13)
- TDC n=41 (m 33, f 8)
- 8-12 years
- Age and IQ matched
- Big tracts:
  - Posterior Thalamic Radiations
  - Posterior Corpus Callosum
  - Posterior Internal Capsule
  - Anterior Thalamic Radiation

White matter microstructure is associated with auditory and tactile processing in children with and without sensory processing disorder.
Yi-Shin Chang[1], Mathilde Gratiot[2], Julia P. Owen[1,], Anne Brandes-Aitken[3], Shivani S. Desai[2], Susanna S. Hill[3], Anne B. Arnett[3], Julia Harris[3], Elysa J. Marco[4,4,5], Pratik Mukherjee[1] ; Fontiers in Neuroscience (submitted and pending review)

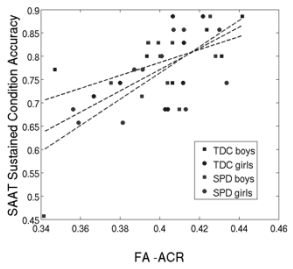
Correlating Bedside & Structure Tactile



Bedside with Structure Auditory



Correlations – Sustained Attention



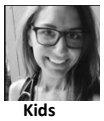
Brain Training
(focus on cognitive control/attention)

Our 3 step approach…
Marco + Gazzaley + Akili Interactive

- Step 1: Assess Challenges
  - parent report, direct assessment, Neuroimaging/EEG
- Step 2:Train with Engaging Platform
  - COLLABORATION WITH PROFESSIONALS!
- Step 3: Reassess for Performance and Plasticity
  - Direct game behavior
  - Transfer skills
  - Neurophysiologic and Structural Change

Step 1: Assess Challenges

- Parent report: Sensory Profile & Vanderbilt
- Direct Assessment:
  - Motor Speed, TOVA, Flanker, Neuroracer
- Neuroimaging: DTI
- Neurophysiology: EEG/Neuroracer



Step 2: Play EVO

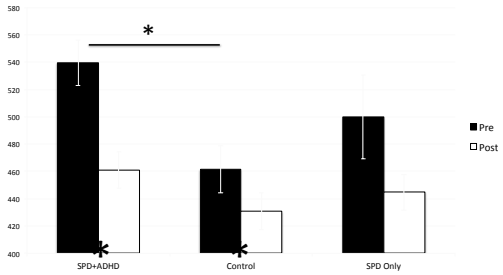
Kids

- n=18 SPD ; n=19 NT
- Age 8-12 y
- PIQ > 70

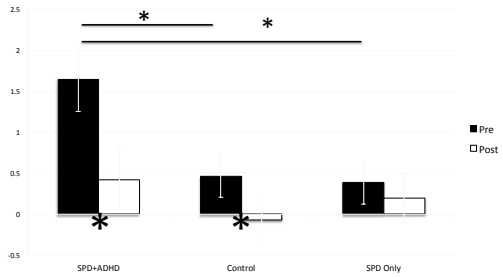
Play

- 7 rounds a day (30 min)
- 20 days of training with driving and targeting
- Challenge assessment at each new world
- 4 worlds total

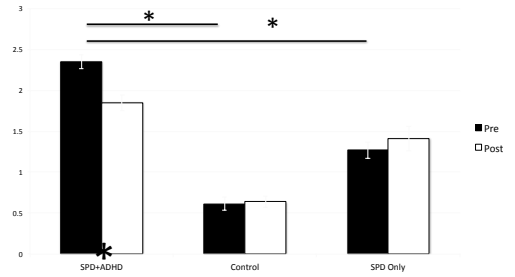
Shoot Only NeuroRacer Condition Direct Game Behavior



TOVA RTV (transfer of skills)

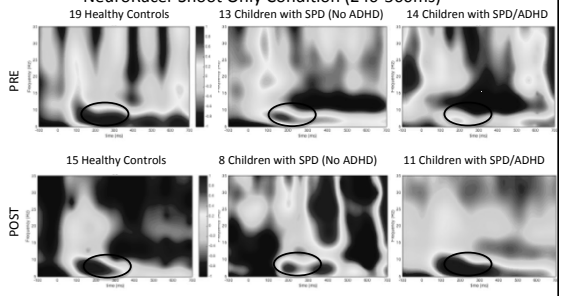


Vanderbilt Average Inattention (real world change?)



Step 3: Performance and Plasticity Midline Frontal Theta Power

NeuroRacer Shoot Only Condition (240-360ms)



So what ever happened to Touchy Tommy?

- Stay Tuned.

Many Hands :

- **The kids and their parents!**
- SPD MEG/DTI Team
  - Srikantan Nagarajan
  - Pratik Mukherjee
  - Elliott Sherr
  - Leighton Hinkley
  - Carly Demopoulos
  - Shivani Desai
  - Ashley Antovich
  - Julia Harris
  - Susannah Hill
  - Richard Hill
  - Angelina Jocson
- Kasra Khatibi
- Anne Bernard
- Monica Arroyo
- Heidi Kirsch
- Anne Findlay
- Suzanne Homna
- Julia Owen
- Shin Chang
- Mathilde Gratiot
- MAC
  - Bruce Miller
  - Joel Kramer
  - John Neuhaus
- Sensory Processing Foundation
  - Lucy Miller
  - Sarah Schoen
- EVO Team
  - Adam Gazzaley
  - Joaquin Anguera
  - Shivani Desai
  - Ashley Antovich
  - Cammie Rolle
  - Johno Gibbons
  - Annie Aiken
  - Sasha

Thank you for your multisensory attention!