

### The New Neuroscience of Two: Breakthrough fNIRS Technology and Emerging Principles of Dyadic Interaction







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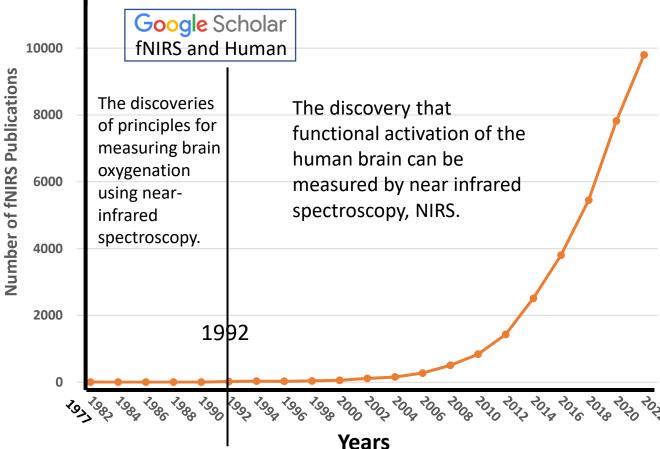


Clare Elwell University College of London, UK



## About the Science by Year

#### Historical Milestones for fNIRS



Jöbsis, F.F., 1977. Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science 198, 1264–1267.

Wyatt, J.S., Cope, M., Delpy, D.T., Wray, S., Reynolds, E.O., 1986. Quantification of cerebral oxygenation and haemodynamics in sick newborn infants by near infrared spectrophotometry. Lancet 2, 1063–1066.

Chance, B., Zhuang, Z., UnAh, C., Alter, C., Lipton, L., 1993. Cognition-activated low frequency modulation of light absorption in human brain. Proc. Natl. Acad. Sci. U. S. A. 90, 3770–3774.

NeuroImage 63 (2012) 921-935



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Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

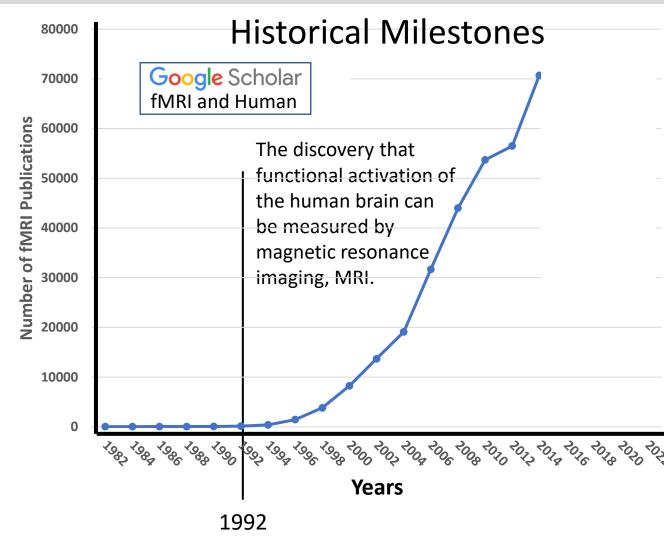


#### Review

A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application

Marco Ferrari \*, Valentina Quaresima Department of Health Sciences, University of L'Aquila, L'Aquila, Italy

## About the Science: fMRI Publications by Year 1992 was a good year for the hemodynamic response function



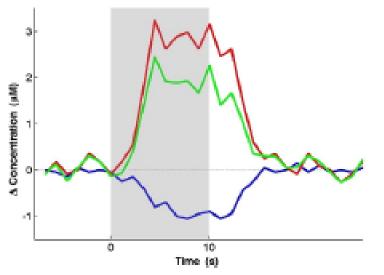
Ogawa, S., Tank, D.W., Menon, R., Ellermann, J.M., Kim, S.G., Merkle, H., Ugurbil, K., 1992. Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. Proc. Natl. Acad. Sci. U. S. A. 89, 5951–5955.

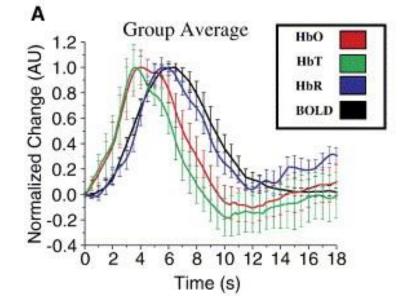
# A Common Physiological basis for functional NIRS and functional MRI signals: the hemodynamic response function

#### The Neurovascular Coupling Principle

Active neural regions of Brain recruit oxygenated blood for metabolic support.

Fig. 2. Sketch of the typical cortical activation as revealed by fNIRS.





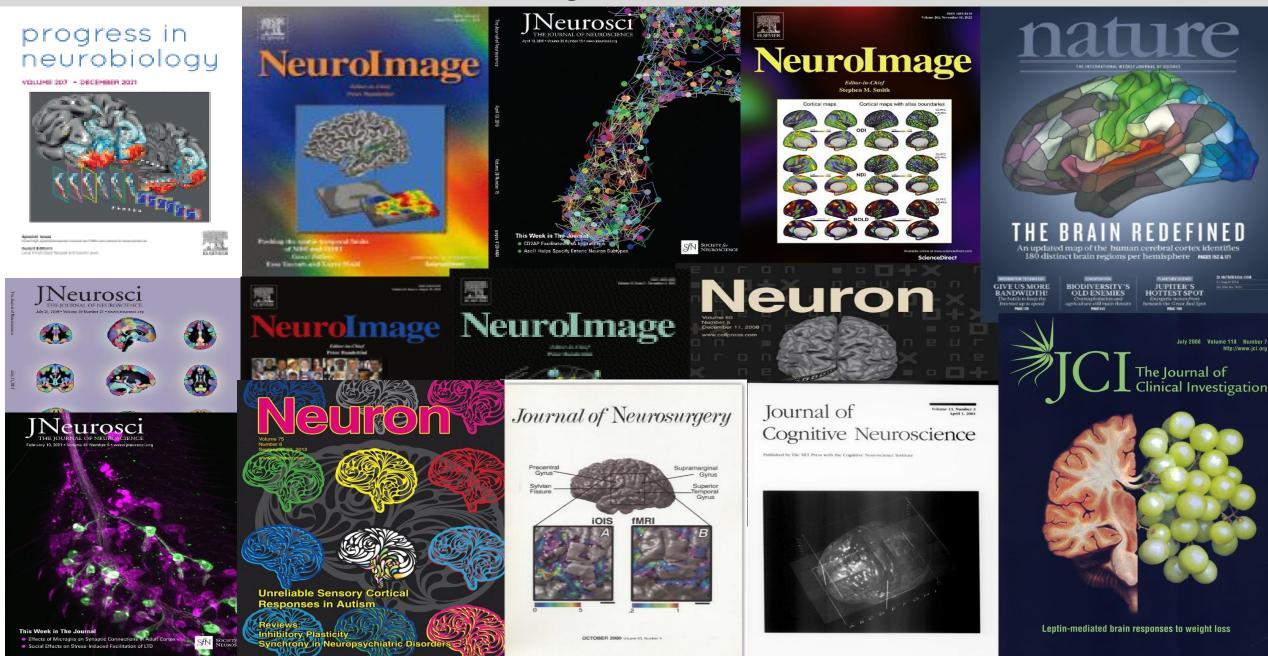
Ferrari, M, Quaresima, V, A brief review on the history of human functional nearinfrared spectroscopy (fNIRS) development and fields of application. NeuroImage 63 (2012) 921–935

Huppert, T. J., Hoge, R. D., Diamond, S. G., Franceschini, M. A., & Boas, D. A. (2006). A temporal comparison of BOLD, ASL, and NIRS hemodynamic responses to motor stimuli in adult humans. *Neuroimage*, *29*(2), 368-382.

Detection of task-activated recruitment of blood serves as a proxy for neural activation and provides a link between behavior and brain function.

The signal is referred to as the hemodynamic response function

#### fMRI Revolutionized Cognitive Neuroscience from 1992



## The **BRAIN** Initiative



National Institutes of Health The vision to understand the operations of the human brain and to conquer the challenges of brain disorders were realized by the NIH BRAIN Initiative.

BRAIN (Brain Research through Advancing Innovative Neurotechnology) https://braininitiative.nih.gov

The initiative was launched on April 2, 2013 by US Pres. Barack Obama who announced a grand challenge to "accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits that interact at the speed of thought."

Subsequently, the NIH introduced a 10 year plan to achieve the primary objective of accelerating the development of technology for acquiring fundamental insights about how the nervous system functions in health and disease.

2013 - 2023

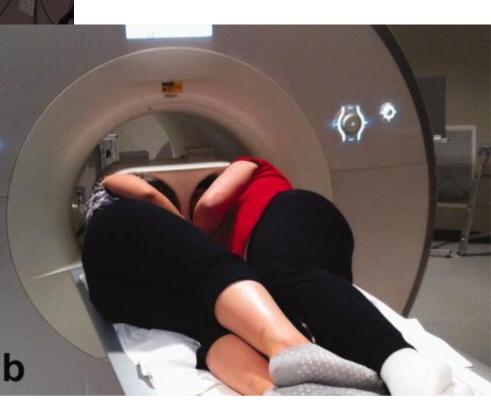


# fMRI Investigations of Human Brain Function are generally limited to a single participant



Montague, P. R., Berns, G. S., Cohen, J. D., Mcclure, S. M., Pagnoni, G., Dhamala, M., et al. (2002). Hyperscanning: simultaneous fMRI during linked social interactions. Neuroimage 16, 1159–1164. doi: 10.1006/nimg.2002.1150

Koike, Takahiko, Hiroki C. Tanabe, and Norihiro Sadato. "Hyperscanning neuroimaging technique to reveal the "two-in-one" system in social interactions." Neuroscience research 90 (2015): 25-32.



Lee, R. F., Dai, W., & Jones, J. (2012). Decoupled circular-polarized dual-head volume coil pair for studying two interacting human brains with dyadic fMRI. Magnetic Resonance in Medicine, 68(4), 1087-1096.

## Humans are Profoundly Social



The underlying neural systems that are associated with live social interactions can not be investigated in a scanner.

#### What to do?





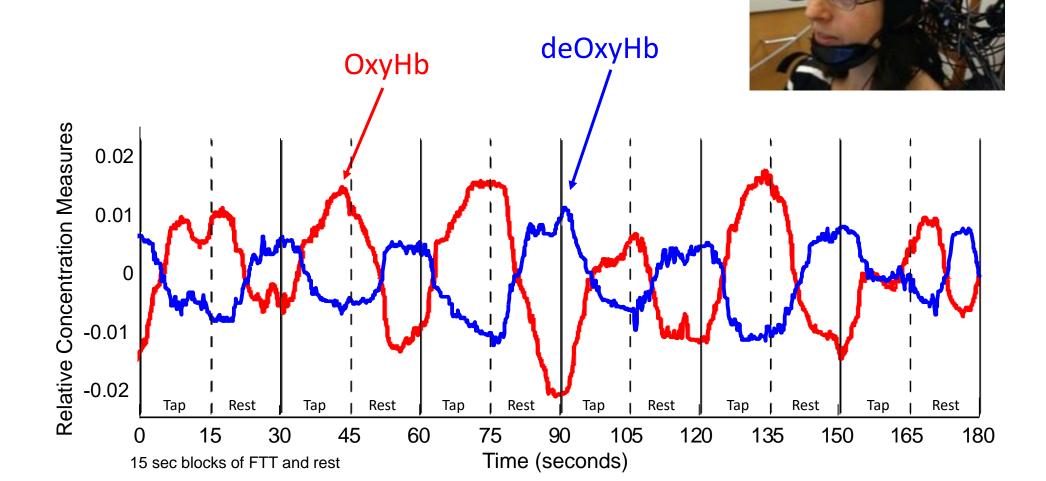
The Brain Function Laboratory 25 Sep 2014

The Brain Function Laboratory 12 Nov, 2014

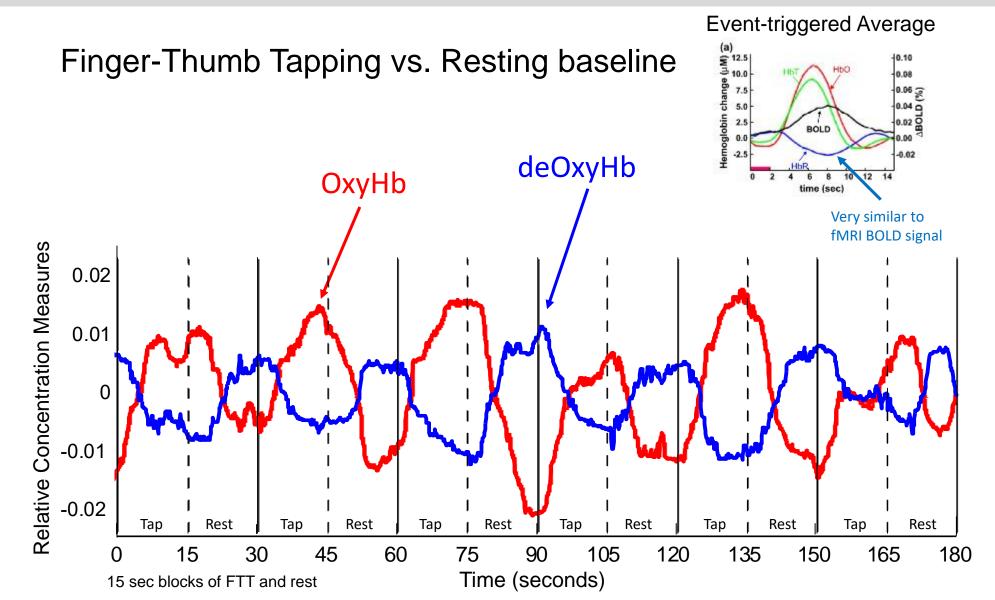
NQ

Hemodynamic signals: OxyHb and deOxyHb Single Subject - Single Run - Single Channel

Finger-Thumb Tapping vs. Resting baseline



## Hemodynamic signals: OxyHb and deOxyHb Single Subject - Single Run - Single Channel



The Brain Function Laboratory 12 Nov, 2014

EXIT

#### From fMRI to fNIRS: From One Brain to Two Brains



#### **fNIRS** features

- Temporal Resolution ≈ 30 msec
- Spatial Resolution ≈ 3 cm (surface and depth)
- No magnetic field or scanner
- Tolerance to motion

#### Simultaneous acquisitions of Multiple Modalities:

- Eyetracking (Tobii Pro X3-120) •
- EEG: g.tec (active electrodes)
- Scene cameras

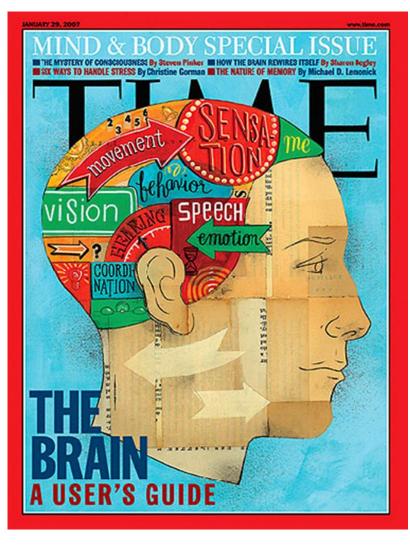
- Facial Classification:
- Behavioral measures
- Physiological measures

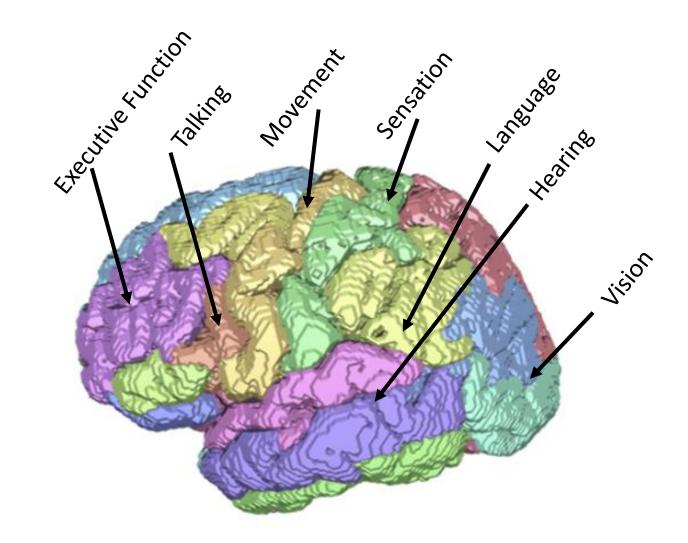
Scholkmann F, Holper L, Wolf U, Wolf M. A new methodical approach in neuroscience: Assessing inter-personal brain coupling using functional near-infrared imaging (fNIRI) hyperscanning. Frontiers in Human Neuroscience. 2013;7:813.

Babiloni F, Astolfi L. Social neuroscience and hyperscanning techniques: Past, present and future. Neuroscience & Biobehavioral Reviews. 2014;44:76-93 Noah JA, Ono Y, Nomoto Y, Shimada S, Tachibana A, Zhang X, Bronner S, Hirsch J: fMRI Validation of fNIRS Measurements During a Naturalistic Task. J Vis Exp. 2015 Jun 15;(100):e52116. doi: 10.3791/52116. PMID: 26132365.

## The Brain "101": First Principle

The Real Estate Principle: The Brain is organized by functional parts

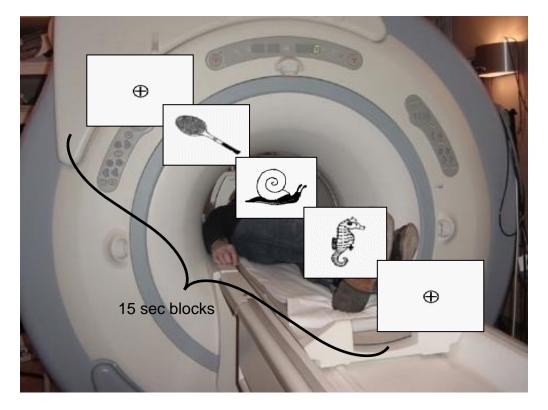


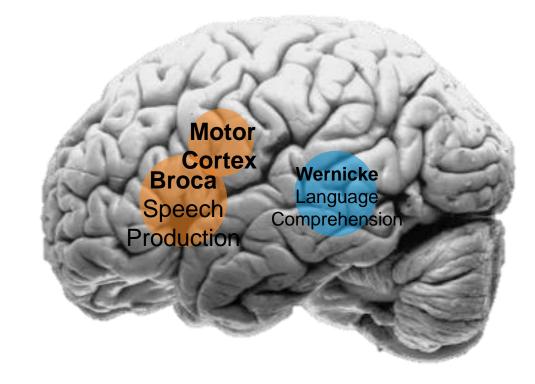


Parker, C. S., Deligianni, F., Cardoso, M. J., Daga, P., Modat, M., Dayan, M., ... & Clayden, J. D. (2014). Consensus between pipelines in structural brain networks. *PloS one*, *9*(10), e111262.

## Real-Estate for Human Language

#### Picture Naming and Description Task (Silent)





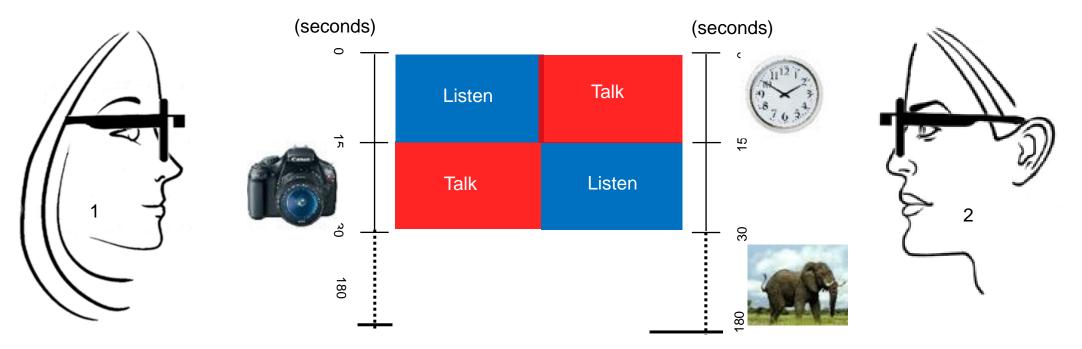
The human language system includes specialized regions for production (talking) and reception/comprehension (listening).

Hirsch, J., R-Moreno, D., & Kim, K. H. S. (2001). Interconnected large-scale systems for three fundamental cognitive tasks revealed by functional MRI. Journal of Cognitive Neuroscience, 13(3), 389-405.

Hirsch, J., Ruge, M. I., Kim, K. H. S., Correa, D. D., Victor, J. D., Relkin, N. R., Labar, D. R., Krol, G., Bilsky, M. H., Souweidane, M. M., DeAngelis, L. M., & Gutin, P. H. (2000). An integrated fMRI procedure for preoperative mapping of cortical areas associated with tactile, motor, language, and visual functions. Neurosurgery, 47(3), 711-722

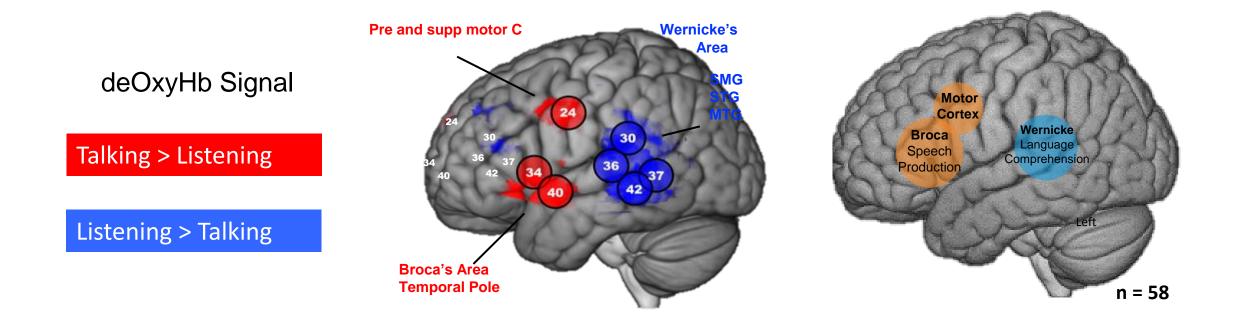
## Validation of Dyadic Functions Two-Person Picture Naming Task using fNIRS

Are Canonical Language Regions Reproducible by fNIRS?



Picture naming and description task (No face-to-face contact)

#### **Two-Person Picture Naming Task**



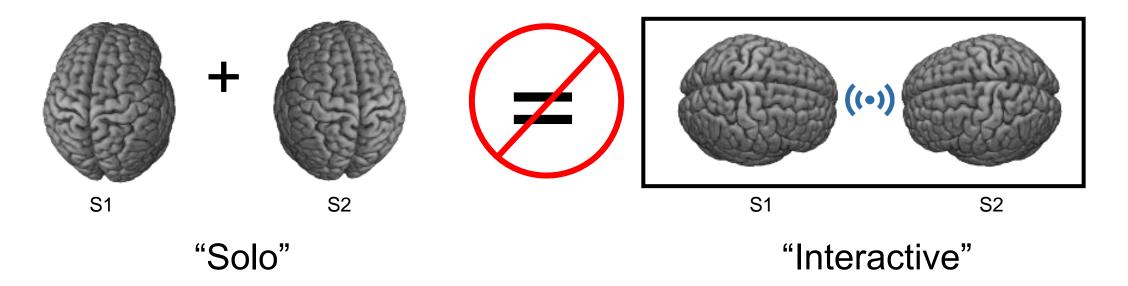
## Expectation for canonical language systems, Broca's Area (red) and Wernicke's Area (blue) is confirmed.

Hirsch, J., Noah, J.A., Zhang, X., Dravida, S., & Ono, Y. (2018). A cross-brain neural mechanism for human-to-human verbal communication. Social Cognitive and Affective Neuroscience, 13(9), 907–920. DOI: 10.1093/scan/nsy070.

## Does Live Social Interaction Matter? A Guiding Hypothesis:

#### The Interactive Brain Hypothesis:

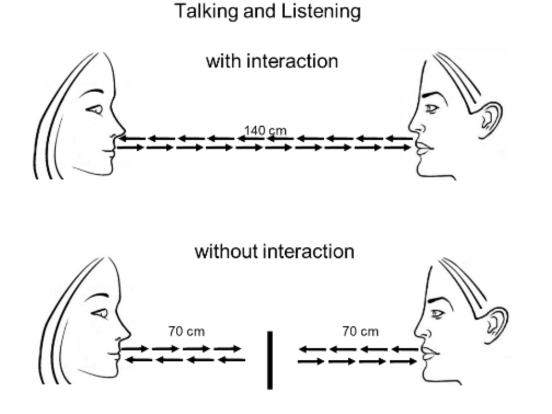
Two dynamically interacting brains engage co-operating neural systems that reciprocally share social information.

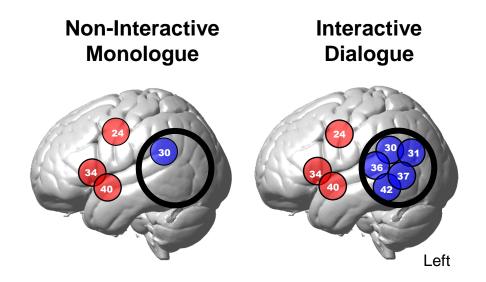


E. Di Paolo & H. De Jaegher. "The interactive brain hypothesis." *Frontiers in Neuroscience* (2012); 6:163.
L. Schilbach, et al. "Toward a second-person neuroscience" *Behavior and Brain Sciences* (2013) 36, 393-462.
Wheatley T, Boncz A, Toni I, Stolk A. Beyond the isolated brain: the promise and challenge of interacting minds. Neuron. 2019;103(2):186-8.

## Interactive vs "Solo" Language: A Test of the Interactive Brain Hypothesis for Language

#### Does Interpersonal Interaction Matter?



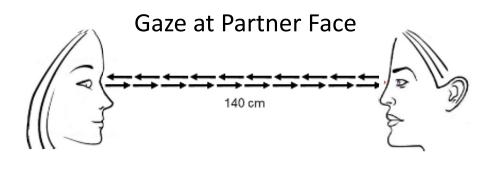


Findings are consistent with the hypothesis that interpersonal interaction matters with respect to language processing in Wernicke's Area.

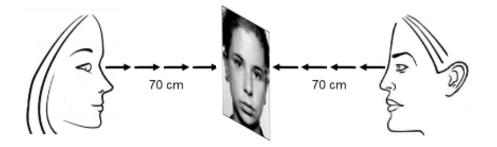
Hirsch, J., Noah, J.A., Zhang, X., Dravida, S., Ono, Y. (2018) A Cross-Brain Neural Mechanism for Human-to-Human Verbal Communication. Social Cognitive and Affective Neuroscience. Volume 13, Issue 9, Pages 907–920. DOI: 10.1093/scan/nsy070.

## A Test of the Interactive Brain Hypothesis for Faces

Eye-Gaze paradigm: "Real" vs Video Picture

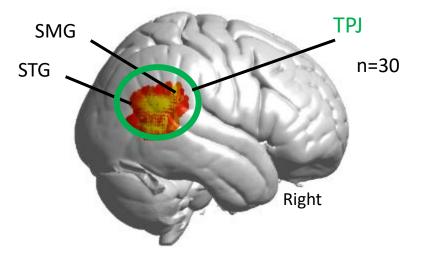


Gaze at Video Face



"Real" > "Video"

[Face-to-Face] > [Video Gaze]



Findings are consistent with the hypothesis that "Realness" matters with respect to human face processing in the right Temporal Parietal Junction.

Noah, J. A., Zhang, X., Dravida, S., Ono, Y., Naples, J. A., McPartland, J. C., & Hirsch, J. (2020). Real-time eye-to-eye contact is associated with cross-brain neural coupling in angular gyrus. Frontiers in Human Neuroscience 14(19), 1-10. doi: 10.3389/fnhum.2020.00019

Hirsch, J.\*, Zhang, X., Noah, J.A., Ono, Y., (2017) Frontal temporal and parietal systems synchronize within and across brains during live eye-to-eye contact, NeuroImage, Volume 157, 15 August 2017, Pages 314-330, ISSN 1053-8119, https://doi.org/10.1016/j.neuroimage.2017.06.018.

#### Yes, the findings are consistent with the Interactive Brain Hypothesis: Live interactions influence brain processes. fNIRS Technology enables a change of focus from the single brain to the dyad:

Neuroimaging two-brains simultaneously during natural and reciprocal interactions



ILLUSTRATION BY BEE JOHNSON

#### The New Neuroscience of Two

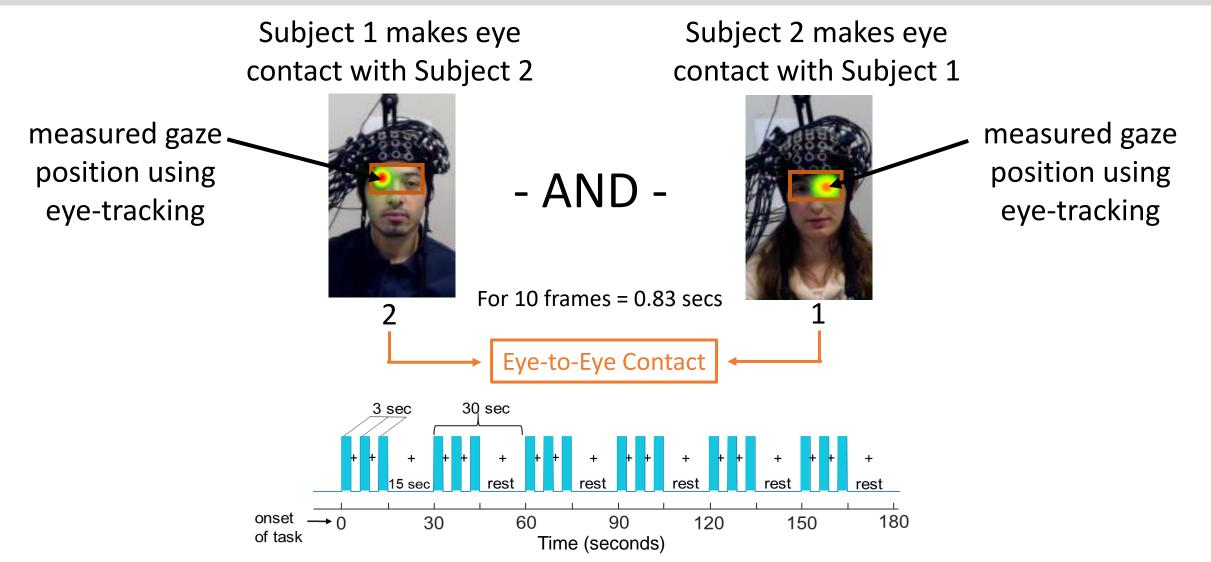
A Foundation for the New Dyadic Neuroscience: Live Interaction Matters. Why?

*"The face is the image of the mind and the eyes are it's interpreter" Cicero, 46 B.C.* 

"Ut imago est animi voltus sic indices oculi"

Cicero's hypothesis: Eyes have special access to the brain and faces are sources of social information. We test this hypothesis

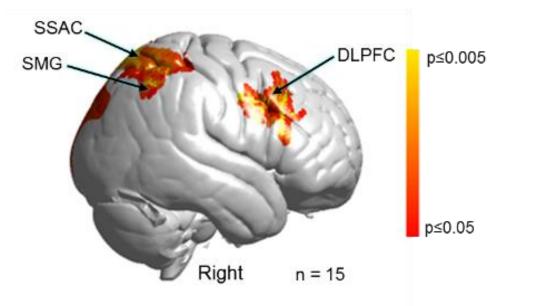
## Measurement of Eye-to-Eye Contact Dual Eye Tracking during face gaze



#### Isolation of Live eye-to-eye contact processing systems in brain

## Eye-Contact co-variate on face-gaze neural data

[Eye-to-Eye] > [Rest] with eye contact co-variate



#### **Finding** A functional network for eye-to-eye contact

"Dorsal Stream"

Right dorsal parietal region

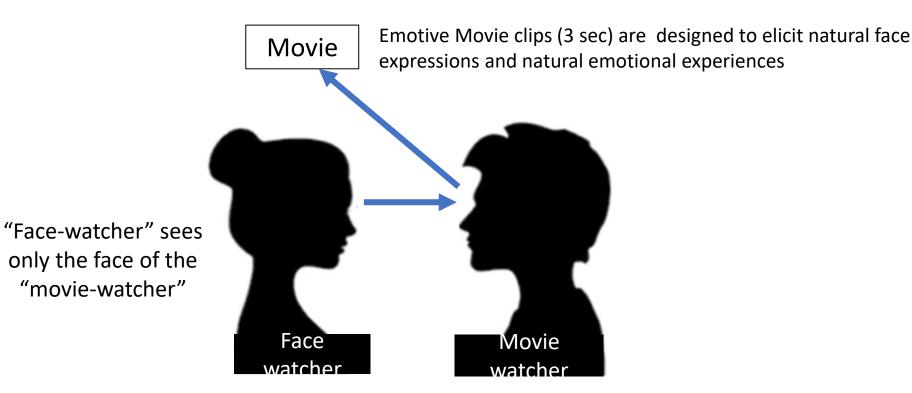
- Somatosensory association Cortex, SSAC
- Supramarginal gyrus, SMG
- Dorsolateral prefrontal Cortex, DLPFC

#### Cicero was right. Eyes and Brain have a special relationship.

Hirsch, J., Zhang, X., Noah, J.A., Naples, A., McPartland, J. (2022) Neural Correlates of Eye Contact and Social Function in Autism Spectrum Disorder. In Press, PLOS ONE.

Why? What does the dorsal region do?: We hypothesize that this dorsal system is engaged during social communication.

#### We test this hypothesis with a new dyadic paradigm



The Dyad: a "MOVIE-WATCHER" and a "FACE-WATCHER"

How we generate "affect" and facial expressions: The "movie-watcher" views emotive movie clips (3 sec) and responds naturally

3 types of affect:

"Adorables"

"Creepies"

"Landscapes"



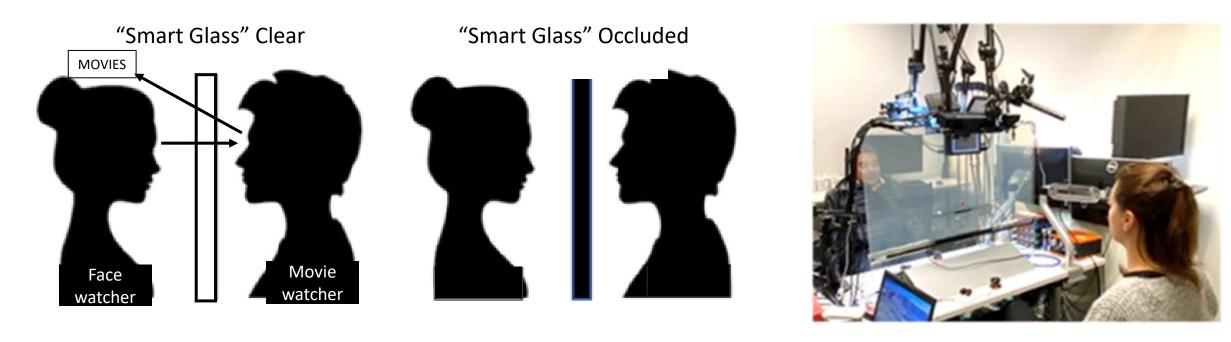


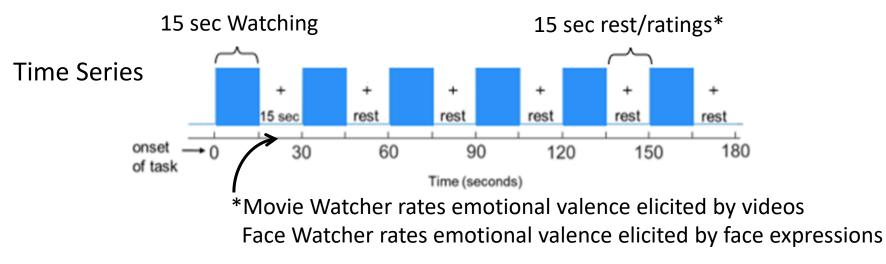
Positive emotion

#### **Negative Emotion**

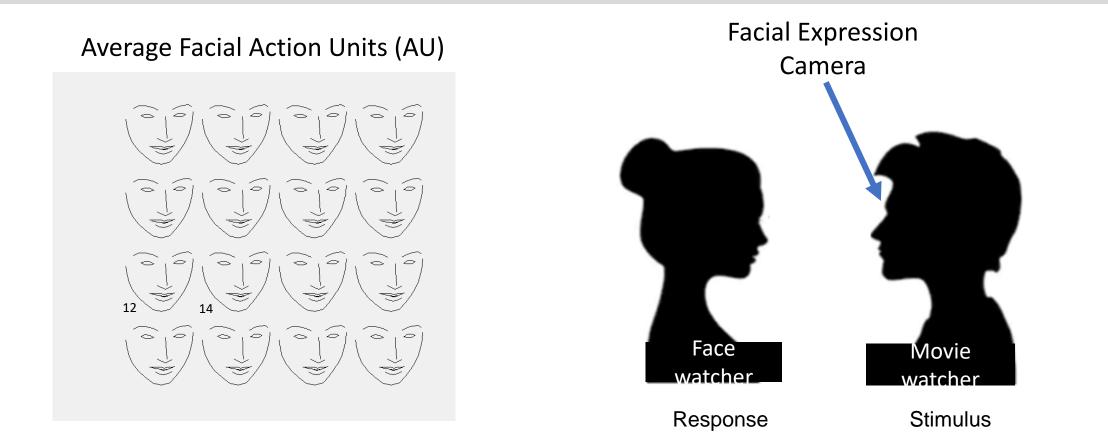
**Neutral Emotion** 

### **Experimental Time Series**





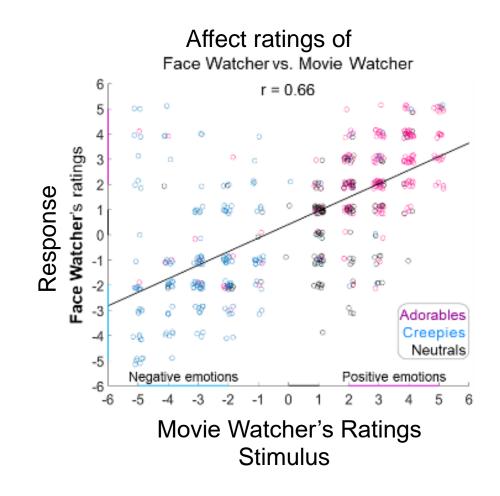
#### Quantification of Facial Expressions Facial Action Units as Natural Facial Expressions of the "Movie-Watcher" are recorded

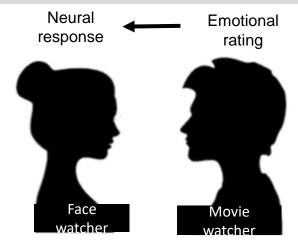


Three dependent variables: Neural responses to face gaze, facial expressions, and affect ratings.

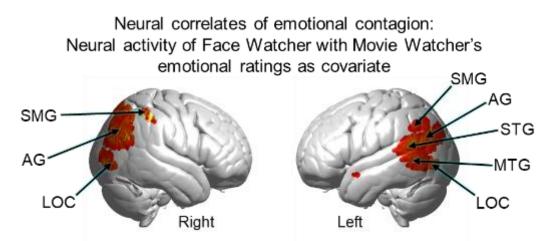
Baltrusaitis, T., Robinson, P. & Morency, L.P. (2016). OpenFace: An open source facial behavior analysis toolkit. Presented at the 2016 IEEE Winter Conference on Applications of Computer Vision (WACV).

#### The transfer of Affect by facial expression. Quantification of Affect conveyed by "Movie Watcher's" Face and Experienced by the "Face Watcher"



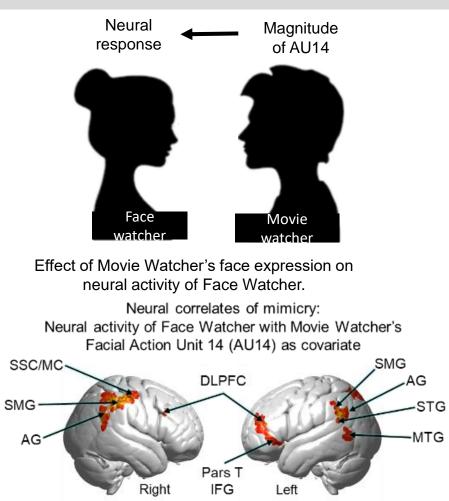


Effect of Movie Watcher's emotional valence and intensity (assessed with ratings) on neural activity of Face Watcher (p <0.05, combined OxyHb and deOxyHb signals).



Joy Hirsch, Xian Zhang, J. Adam Noah, Aishwarya Bhattacharya. Spontaneous mimicry of live facial expressions: A biological mechanism for emotional contagion. 2022, Submitted, Philosophical Transactions of the Royal Society B.

# "Facial expressions" with emotional information are associated with Dorsal stream activity



Wrap up: Dorsal-parietal systems that process social cues have become new regions of interest.

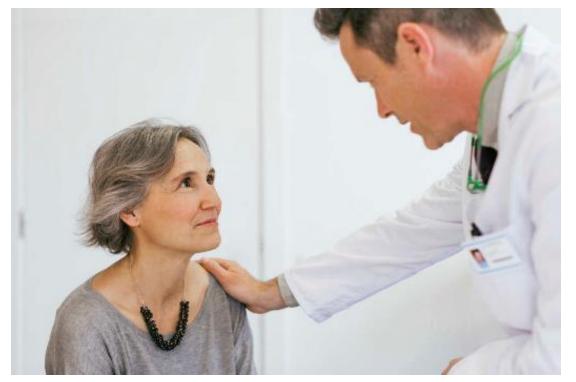
These new systems are relevant to clinical conditions of social disability, and basic neuro-function.

Hirsch, J, Zhang, X, Noah, JA, Bhattacharya, A. Spontaneous mimicry of live facial expressions: A biological mechanism for emotional contagion. 2022, Submitted, Philosophical Transactions of the Royal Society B.

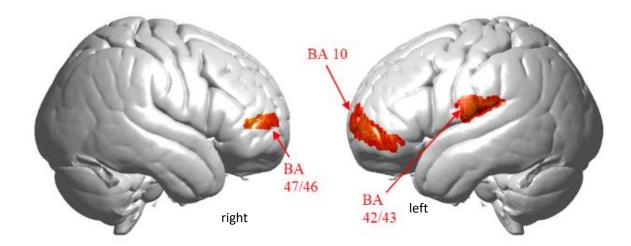
Hirsch, J., Zhang, X., Noah, J.A., Naples, A., McPartland, J. (2022) Neural Correlates of Eye Contact and Social Function in Autism Spectrum Disorder. In Press, PLOS ONE.

# Beyond "neural mechanisms" is there evidence that the type of dyad matters?

The Care-giver vs typical interactions



Frontal Systems of caregivers are associated with the cultivation of mental health for patients



Findings are consistent with the hypothesis that brain activity during dyadic care-giving is frontal pole-specific

**Dyadic Interactions Matter** 

Crum, J., Zhang, X., Noah, J. A., Hamilton, A., Tachtsidis, I., Burgess, P., & Hirsch, J. (2022). An approach to neuroimaging interpersonal interactions in mental health interventions. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, Volume 7, Issue 7, 2022, Pages 669-679, ISSN 2451-9022, https://doi.org/10.1016/j.bpsc.2022.01.008.

## The Social Dyad

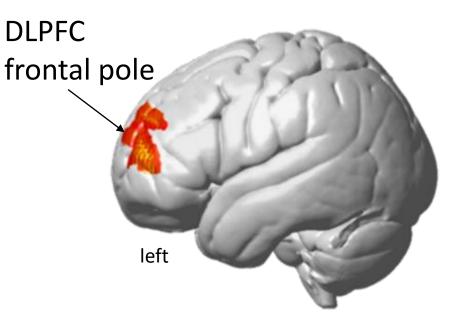
#### High vs Low SocioEconomic Disparity

Conversations between dyads with high socioeconomic disparity vs low socio-economic disparity



**Dyadic Interactions Matter** 

High disparity dyads increase activity in left frontal areas during conversation



Findings are consistent with the hypothesis that brain activity during dyadic spoken interactions depends on who you're talking to.

Olivia Descorbeth, Xian Zhang, J Adam Noah, Joy Hirsch, (2020) Neural processes for live pro-social dialogue between dyads with socioeconomic disparity, Social Cognitive and Affective Neuroscience, nsaa120, https://doi.org/10.1093/scan/nsaa120

## The Social Dyad

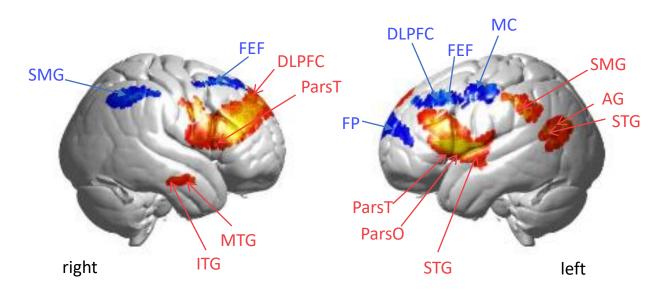
#### Agreement vs Disagreement

Conversations between dyads in Agreement vs Disagreement



#### **Dyadic Interactions Matter**

#### Talking During Disagreement (Red) and Agreement (Blue) activate separate neural systems



Findings are consistent with the hypothesis that brain activity during face-to-face spoken interactions depends on alignment of attitudes.

Hirsch, J., Tiede, M., Zhang, X., Manteau, A., Biriotti, M. (2021). The neurobiology of interpersonal agreement and disagreement during face-to-face dialogue. Frontiers in Human Neuroscience, 14, 606397.

## A Unique property of dyads: Neural Coupling

Neural Coupling is the extent to which the neural responses across brains are synchronous.

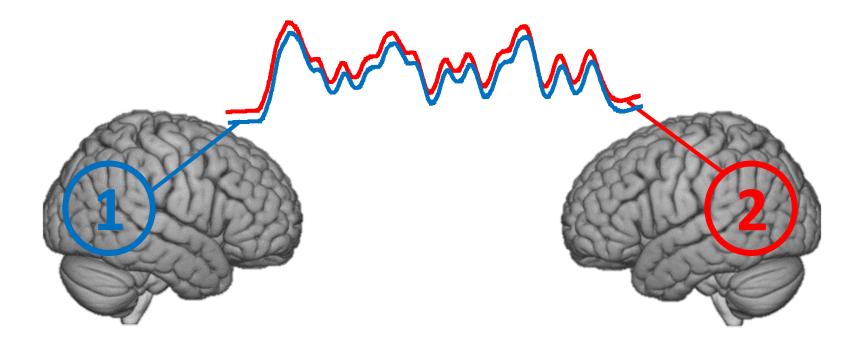
Cui X, Bryant DM, Reiss AL. NIRS-based hyperscanning reveals increased interpersonal coherence in superior frontal cortex during cooperation. Neuroimage. 2012;59(3):2430-7.

Hasson, U., Nir, Y., Levy, I., Fuhrmann, G., & Malach, R. (2004). Intersubject synchronization of cortical activity during natural vision. science, 303(5664), 1634-1640.

Hasson, U., & Frith, C. D. (2016). Mirroring and beyond: Coupled dynamics as a generalized framework for modelling social interactions. Philosophical Transactions of the Royal Society B: Biological Sciences, 371(1693), 20150366.

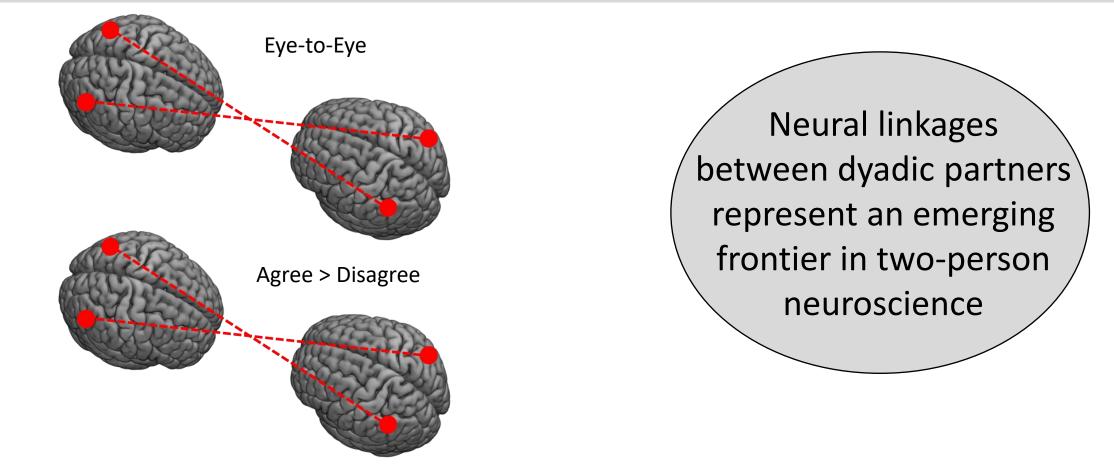
## The Dynamic Neural Coupling Hypothesis:

Dynamic neural coupling: A time series of neural signals originating from a region in brain 1 is coherent with a time series originating from a region in brain 2.



This synchronous relationship is often measured by wavelet analysis.

Neural Coupling: Specialized Neural Mechanisms are dynamically coupled across brains during the exchange of social signals.



Noah, J. A., Zhang, X., Dravida, S., Ono, Y., Naples, J. A., McPartland, J. C., & Hirsch, J. (2020). Real-time eye-to-eye contact is associated with cross-brain neural coupling in angular gyrus. Frontiers in Human Neuroscience 14(19), 1-10. doi: 10.3389/fnhum.2020.00019

Hirsch, J., Tiede, M., Zhang, X., Noah, J. A., Manteau, A., & Biriotti, M. (2021). The neurobiology of interpersonal agreement and disagreement during face-to-face dialogue. *Frontiers in Human Neuroscience*, *14*, 606397.

#### What's the News?

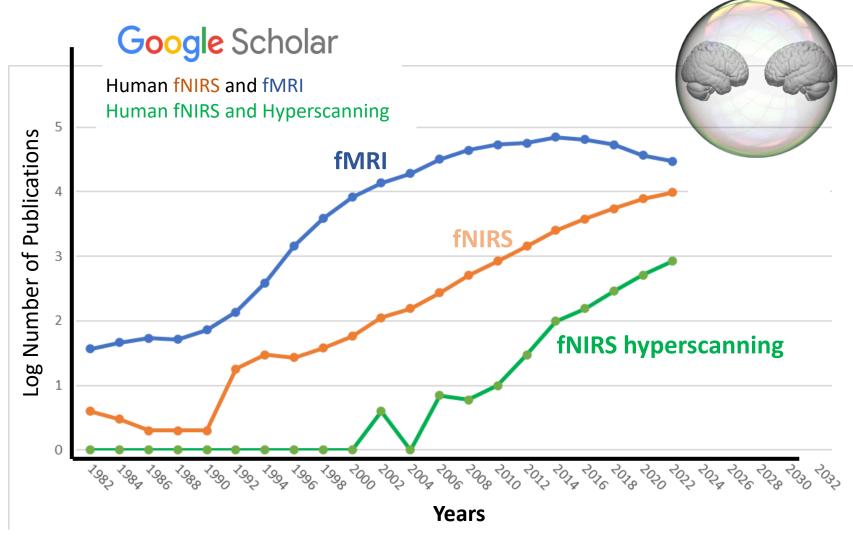


- Dyadic interactions are the Fundamental Unit of behavior
- We introduce both experimental paradigms and computational techniques using fNIRS to measure this new dimension of brain function.
- 3. The principle of neural specificity also applies to dynamic social interactions which may be relevant to social disorders and psychiatric conditions.

1.

4. Neural Coupling between interacting brains represents the development of a new biological component of communication.

## What's Ahead for fNIRS and two-person neuroimaging?



- A mainstream science of dynamic interactions with a proven track record and standards\*
- 2. Theoretical frameworks to guide our hypotheses
- Clinical applications that include understanding of developmental disorders of social interaction
- 4. Solid funding sources
- Continued development of technical infrastructure for twoperson neuroimaging in natural conditions including multi modal approaches.
- A journal that reports and archives scientific advances in two-person neuroimaging

\* Yücel M, Lühmann A, Scholkmann F, Gervain J, Dan I, Ayaz H, et al. Best practices for fNIRS publications. Neurophotonics. 2021;8(1):012101.

2022 Neurophotonics Status Report Highlights optical spectroscopy imaging methods relevant to noninvasive human brain studies

## Vol. 9 / No. 52 NEUROPHOTONICS Optical imaging and spectroscopy for the study of the human brain: status report SPIE

**Corresponding Authors:** Rickson Mesquita Erin M. Buckley

#### **59 Sections:**

- Hardware Development
- Data Analysis and Algorithms
- Functional Applications in Neurodevelopment and Cognition
- Clinical Applications in Optical Spectroscopy and Imaging

Standing on the shoulders of giants within the SfNIRS community, who build the measurement infrastructure, we launch a new "Neuroscience of Two".



Have a great meeting!





**Brain Function Lab Presentations** 

2022 Society for functional NIRS Biennial Meeting Boston, MA



- 1. Adam Noah, Xian Zhang, Mark Tiede, David Ostry & Joy Hirsch Using fNIRS and TMS to detect and disrupt changes in visual processing of faces. PS1\_68\_123.
- 2. Xian Zhang, J. Adam Noah, J. McPartland, Joy Hirsch. <u>FNIRS responses to eye-to-eye contact predict ASD using support vector machine learning</u>. PS1\_70\_128.
- **3.** Megan. Kelley, X. Zhang, J. A. Noah, T. Parker, J. Hirsch. Combined eye-tracking, fNIRS, and EEG suggests eye movements impact neural processing during real face viewing. PS2\_57\_216.
- 4. Termara C. Parker, X. Zhang, J.A. Noah, M.S. Kelley, J.C. McPartland, and J. Hirsch. Neural processing of social gaze cueing in typical and ASD adults during a live face-to-face joint attention task. OS4\_01\_226
- **5. Uz. Hakim**, J.A. Noah, X. Zhang, P. Pinti, J. Hirsch, I.Tachtsidis. <u>Comparing pre-processing pipelines for fNIRS data</u>. PS3\_08\_238.
- 6. Uz. Hakim, J.A. Noah, X. Zhang, P. Pinti, A. Hamilton, J. Hirsch, I. Tachtsidis. <u>Neural Underpinnings of Face Processing During Online Video Calling</u>. PS1\_84\_236.
- **7.** Nan. Zhao, X. Zhang, J.A. Noah, M. Tiede, and J. Hirsch. <u>Comparison of "Live" and "Virtual" Formats for Face Gaze: A Multimodal Investigation</u>. PS3\_61\_334.
- 8. Mark Tiede, Juliana Brenner, J. Adam Noah, Xian Zhang & Joy Hirsch <u>Neural and Behavioral Responses to Talking Faces in Noise</u>. PS1\_55\_96.
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