Emergence of Self :

Development of Social Cognition from Perinatal Period

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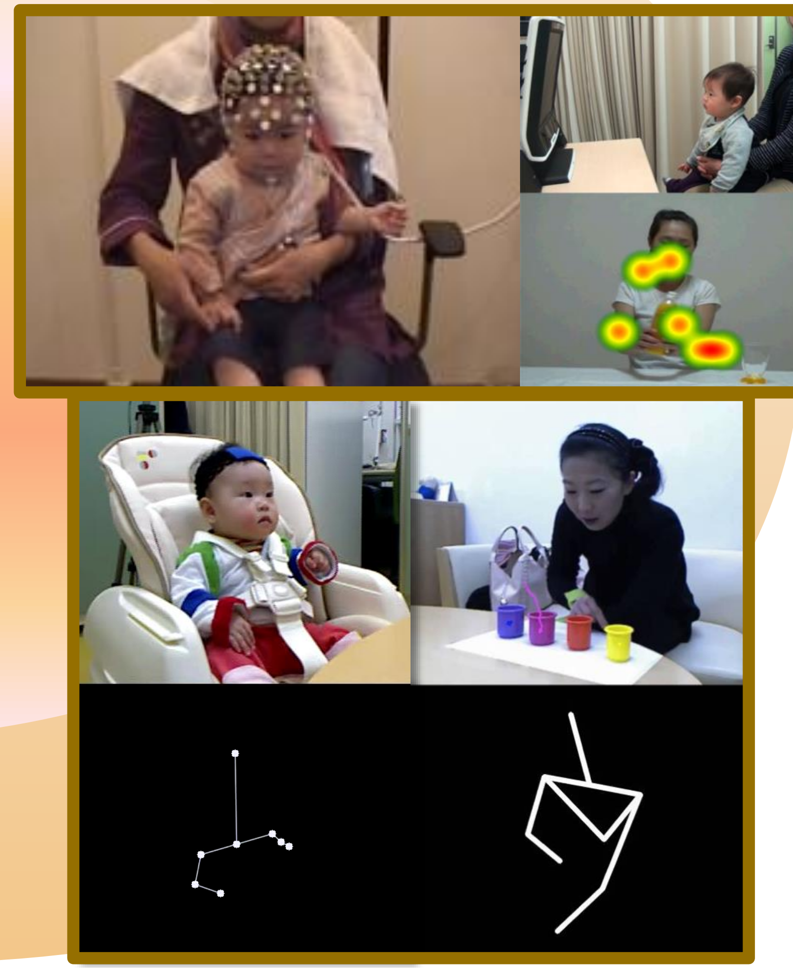
Kyoto University Hospital

Comparative perspective: Chimpanzee research

Kyoto University Baby Lab



Research Questions

toward an understanding of human mind --→ consciousness

1. *What does distinguish the mind of humans from that of other animals?*

   - **Evolutional foundation**

2. *How does the human mind develop?*

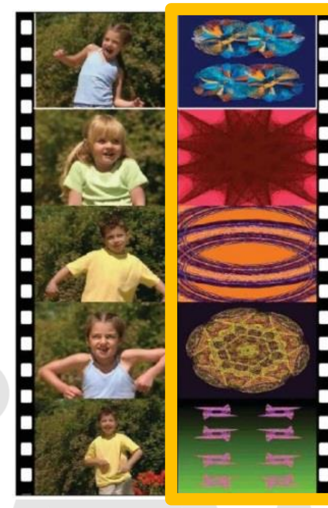
   - **Ontogeny**

3. *What causes* ***typical/atypical*** *development?*

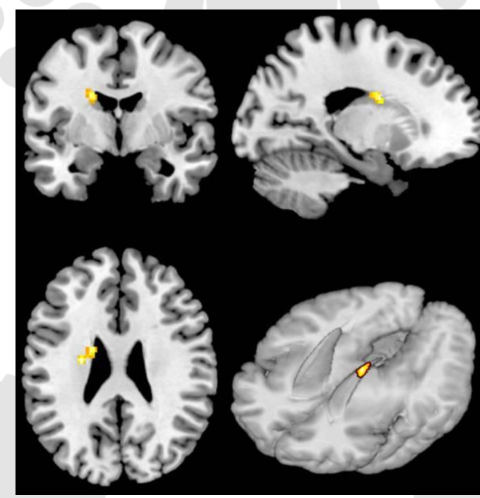
   - **Developmental model of human cognition**

Social and communicative deficits of autism spectrum disorders (ASD)

- ✓ **Persistent deficits in social communication and social interaction across contexts**
  (DSM-V Criteria A)



- ✓ Reward processing abnormalities in ASD are specific to **social stimuli**
  (no difference for monetary rewards)
  - Anterior cingulate vortex (ACC)
  - Ventral striatum
  - Ventral prefrontal cortex



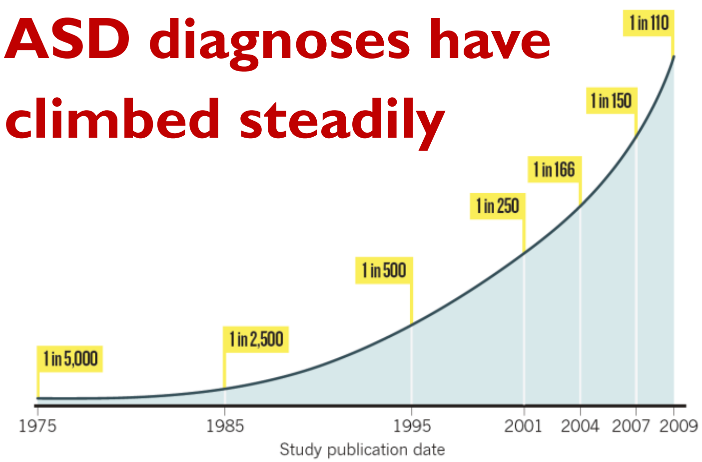
- ✓ Abnormal functional activation and atypical structures of the Amygdala

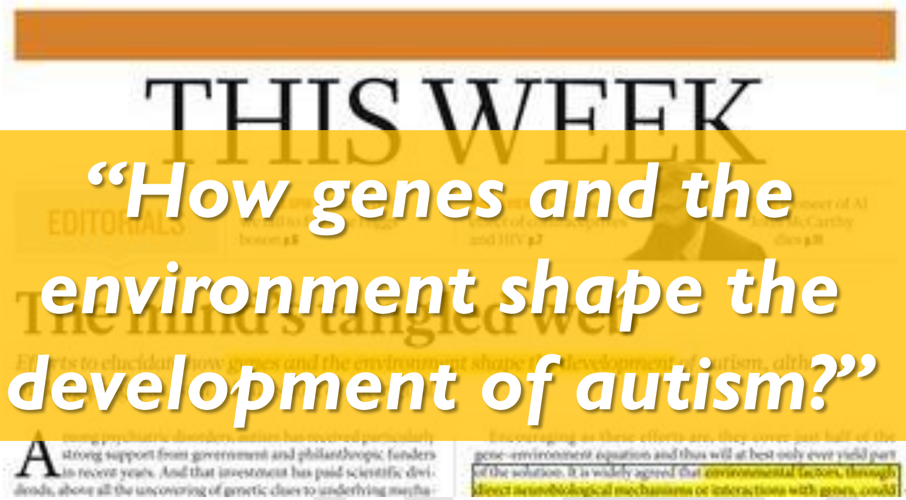
- ✓ "Mirror neuron system" deficit ?

***When* and *Why* such atypicality emerge in ASD?**

The number of ASD children increases
Nature (2011)

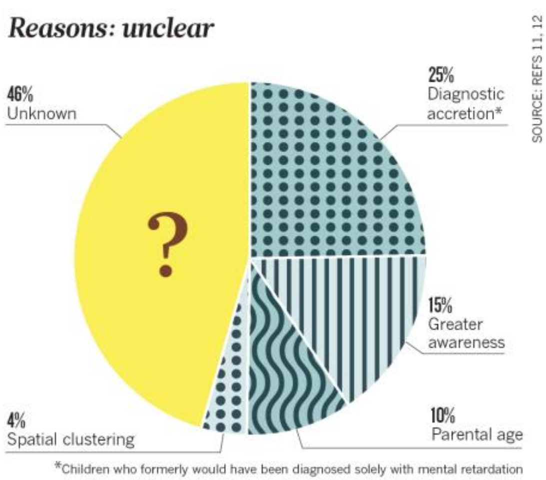
ASD diagnoses have climbed steadily





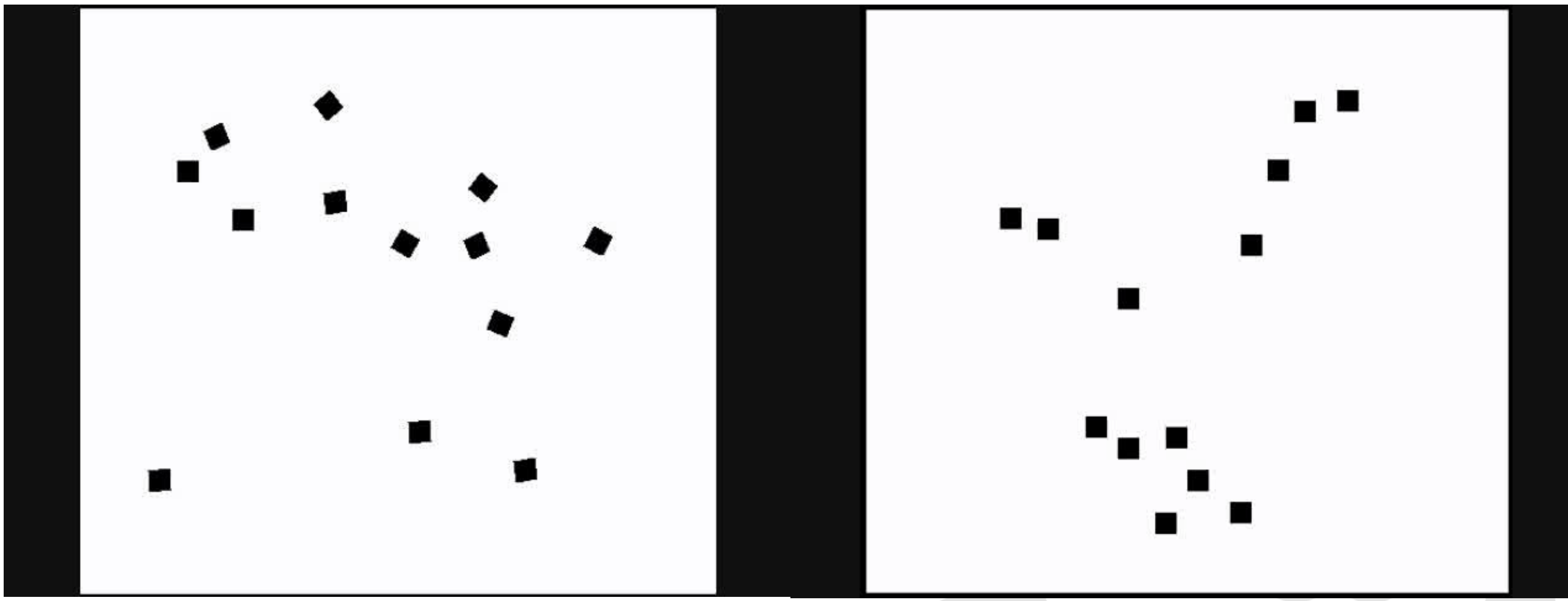
"How genes and the environment shape the development of autism?"

Reason is unclear



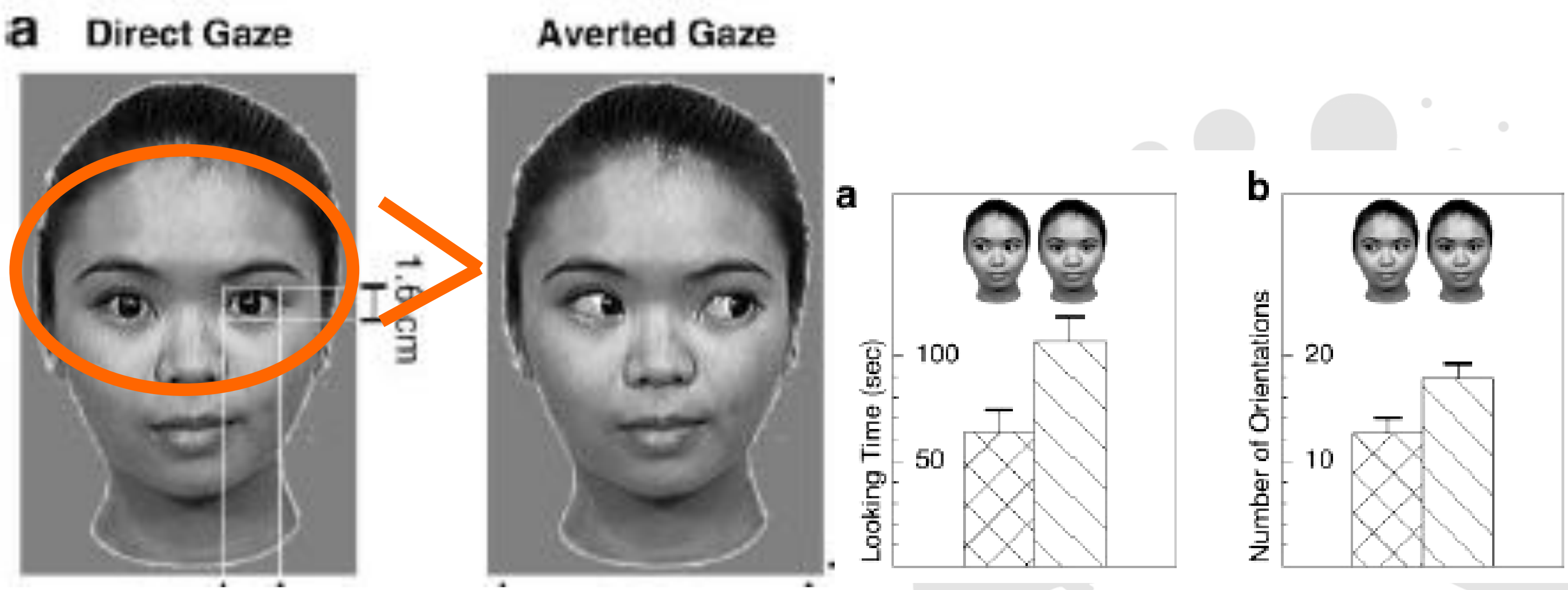
- ✓ **The growth in the prevalence of autism cannot be explained only by genes**
- ✓ **Need to elucidate *the true environmental influences*** on ASD **(gene–environment interactions)**
- ✓ **From fetal period**

Newborns prefer biological motion



Simion et al., 2008, *PNAS*

Newborns prefer faces looking *directly* at them



Farroni et al. 2002, *PNAS*

Infants with ASD decrease attention to eyes from 2 to 6 months of age

LETTER

doi:10.1038/nature12715

Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism

Warren Jones[1,2,3] & Ami Klin[1,2,3]

Deficits in eye contact have been a hallmark of autism[1,2] since the condition's initial description[3]. They are cited widely as a diagnostic feature[4] and figure prominently in clinical instruments[5]; however, the early onset of these deficits has not been known. Here we show in a prospective longitudinal study that infants later diagnosed with autism spectrum disorders (ASDs) exhibit mean decline in eye fixation from 2 to 6 months of age, a pattern not observed in infants who do not develop ASD. These observations mark the earliest known indicators of social disability in infancy, but also falsify a prior hypothesis: in the first months of life, this basic mechanism of social adaptive action—eye looking—is not immediately diminished in infants later diagnosed with ASD; instead, eye looking appears to begin at normative levels prior to decline. The timing of decline highlights a narrow developmental window and reveals the early derailment of processes that would otherwise have a key role in canalizing typical social development. Finally, the observation of this decline in eye fixation—rather than outright absence—offers a promising opportunity for early intervention that could build on the apparent preservation of mechanisms subserving reflexive initial orientation towards the eyes.

Autism Spectrum Disorders (ASDs) affect approximately 1 in ...

Data were collected at 10 time points: at months 2, 3, 4, 5, 6, 9, 12, 15, 18 and 24. We studied 110 infants, enrolled as risk-based cohorts: $n = 59$ at high-risk for ASD (full siblings of a child with ASD[17]) and $n = 51$ at low-risk (without first-, second- or third-degree relatives with ASD). Diagnostic status was ascertained at 36 months. For details on study design, clinical characterization of participants, and experimental procedures, see Methods and Supplementary Information.

Of the high-risk infants, 12 met criteria for ASD[18] (10 males, 2 females), indicating a conversion rate of 20.3%[17]. One child from the low-risk cohort was also diagnosed with ASD. Given the small number of girls in the ASD group, we constrained current analyses to males only, 11 ASD (10 from the high-risk cohort and 1 from the low-risk), and 25 typically developing (all from the low-risk cohort).

At each testing session, infants viewed scenes of naturalistic caregiver interaction (Fig. 1a, b) while their visual scanning was measured with eye-tracking equipment. The 36 typically developing and ASD children viewed 2,384 trials of video scenes.

Control comparisons tested for between-group differences in attention to task and completion of procedures. There were no between-group differences in duration of data collected per child (typically developing = 71.25 (27.66) min, ASD = 64.16 (30.77) min, data given

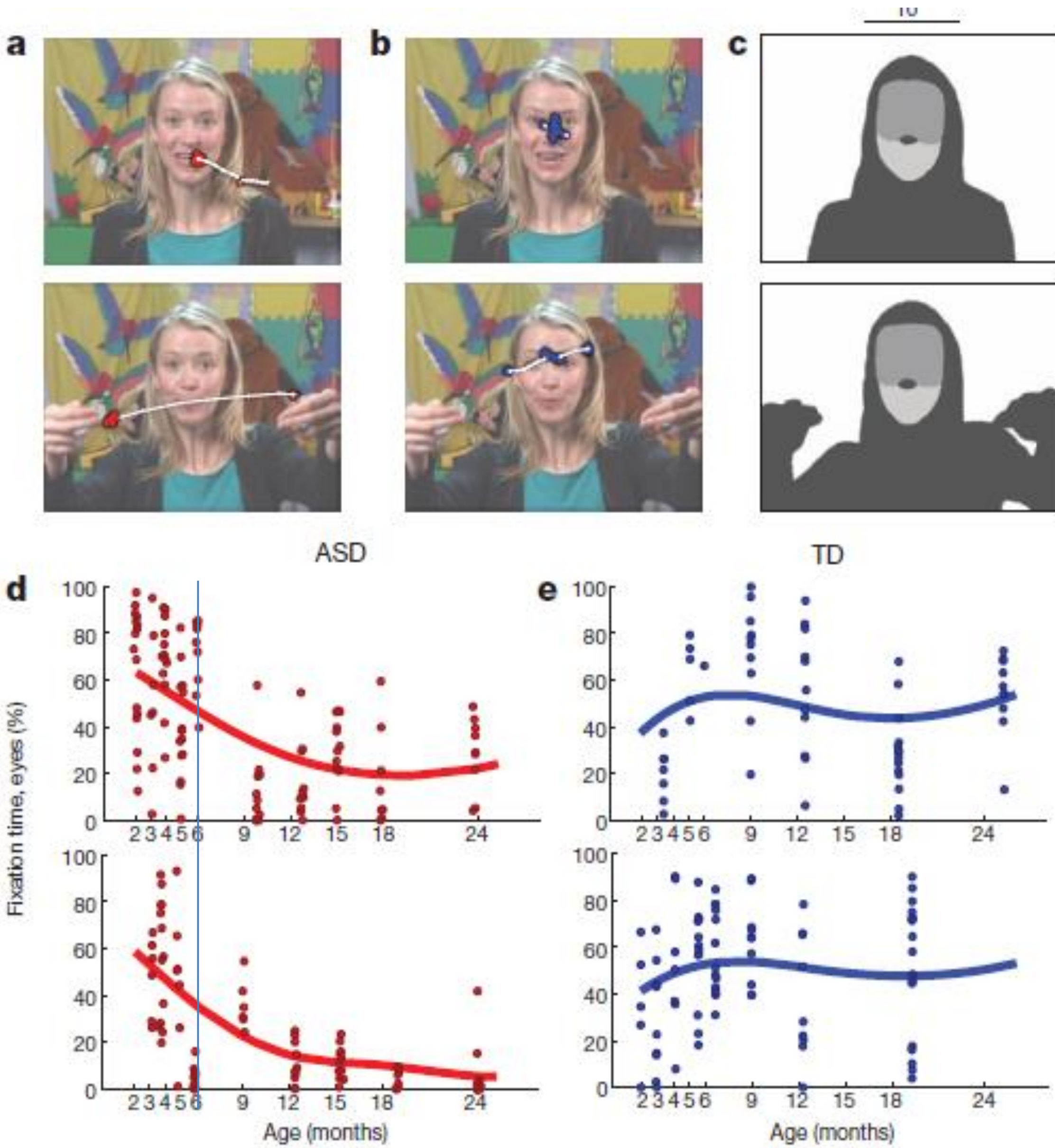


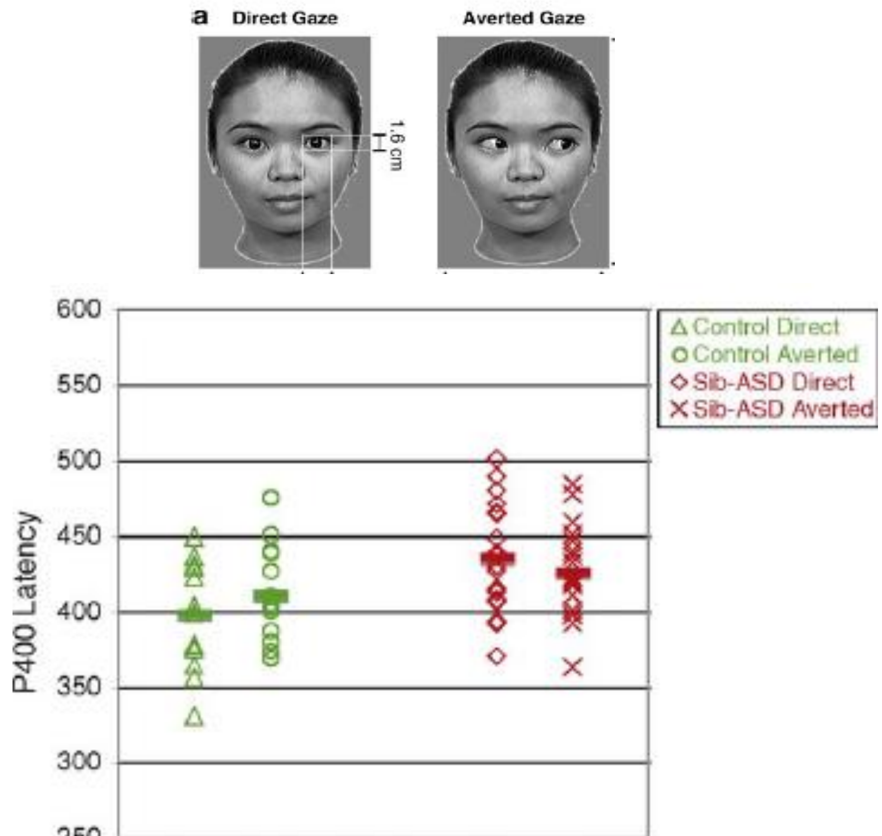
Figure 1 | Example stimuli, visual scanpaths, regions-of-interest, and longitudinal eye-tracking data from 2 until 24 months of age. **a**, Data from a 6-month-old infant later diagnosed with ASD, red. **b**, Data from a typically developing (TD) 6-month-old infant, blue. Two seconds of eye-tracking data are overlaid on each still image, onscreen at the midpoint of the data sample. Saccades are plotted as thin white lines with white dots; fixation data are plotted as larger coloured dots. **c**, Corresponding regions of interest for each image in **a** and **b**, shaded to indicate eye, mouth, body and object regions. **d**, **e**, Trial data with FDA curve fits plotting percentage of total fixation time on eyes, from 2 until 24 months of age, for two children with ASD (**d**) and two TD children (**e**).

Review

Getting answers from babies about autism

Mayada Elsabbagh and Mark H. Johnson

Centre for Brain and Cognitive Development, Birkbeck, University of London, Henry Wellcome Building, London, WC1E 7HX, UK



TRENDS in Cognitive Sciences

Cortical activation in response to various sensory stimuli in newborns

- Near-infrared spectroscopy (NIRS)

Noninvasive blood oxygenation monitoring

- Produce a new NIRS headgear covering the entire head
  (the occipital, temporal, centroparietal areas)

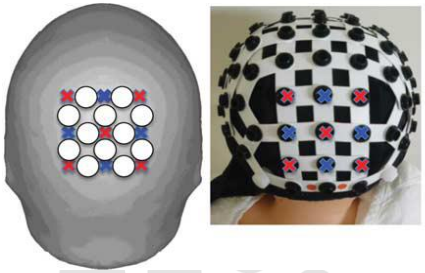
- No studies measure brain activities over broad cortical areas for various sensory stimuli with the same probe

Novel NIRS headgears covering the whole newborn brain

Shibata et al. 2012, *NeurorReport*

Three types of sensory stimuli

- **Auditory** : noise, speech, piano music, female voice
- **Visual** : flashing light at 8-20Hz
- **Tactile** : vibration motor



43 channels

JST 独立行政法人 科学技術振興機構 Japan Science and Technology Agency

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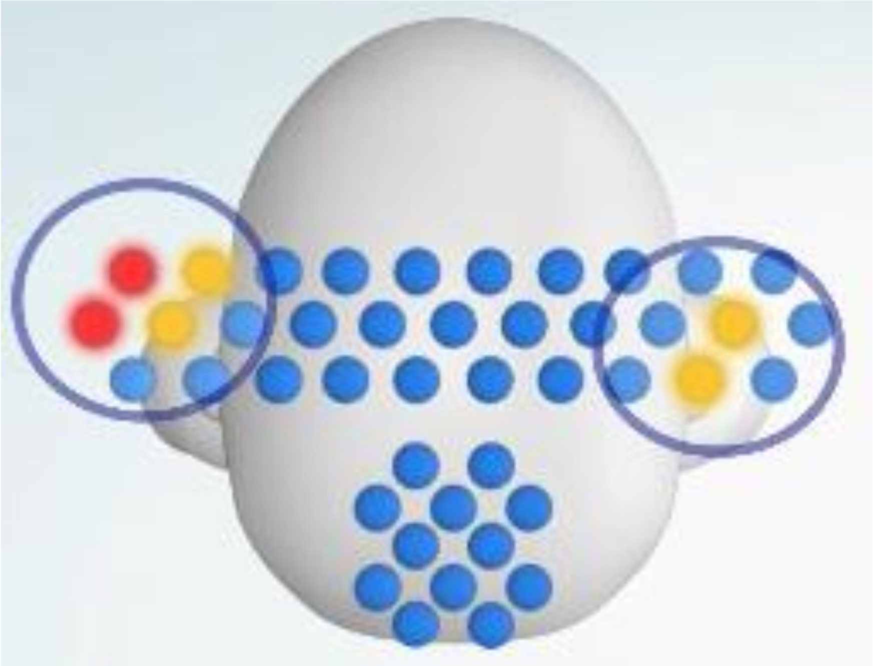
Auditory task



Right / Left temporal areas

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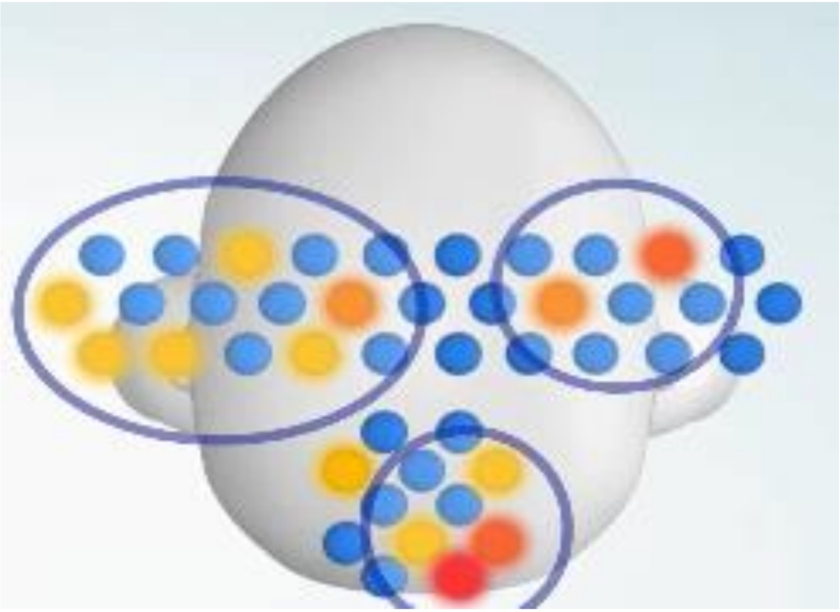
Visual task



Occipital and some Temporal areas

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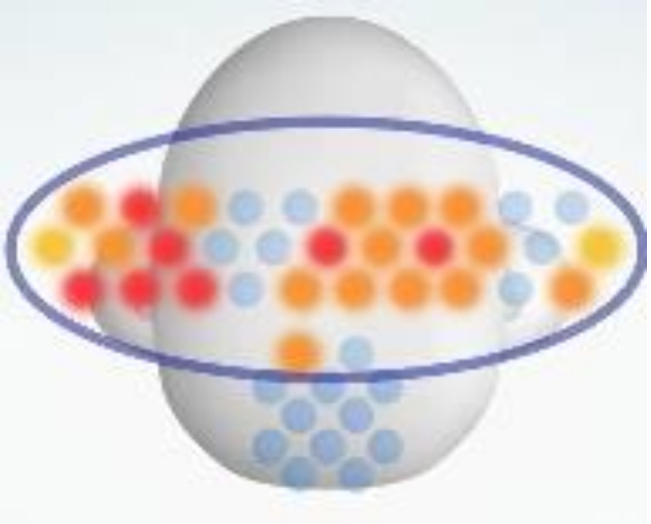
KYOTO UNIVERSITY FOUNDED 1897 KYOTO JAPAN

Tactile task



Right/Left temporal and centroparietal areas

Tactile experience is important in early development

- Different types of stimuli activate each corresponding primary sensory cortex
- Tactile stimuli activate in broader brain areas compared with other types of stimuli
- Importance of tactile sensation in the perinatal period

独立行政法人 科学技術振興機構 JST Japan Science and Technology Agency

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Observation of human fetus using four-dimensional ultrasound sonography

Scanning fetal **body movements** and **facial expression** with 3-D imaging in almost real-time mode (20 frames /sec.)

Human fetuses begin to learn

- Toward the "*external world*"

  - Pushing womb wall by their palm (25 w GA)

  - Grasping umbilical cord by their fingers (30 w GA)

- Toward "*their own body*"

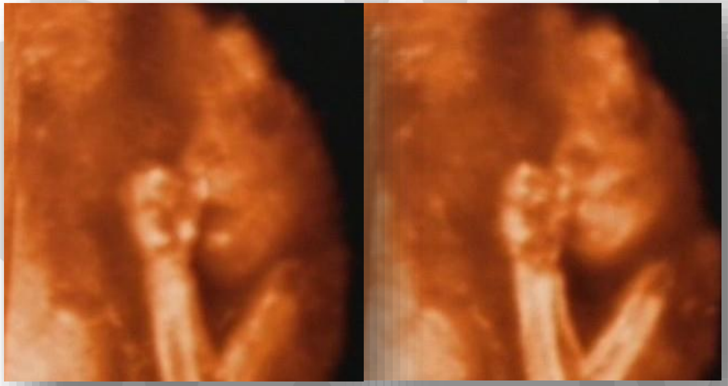
  - Hands to mouth (18 w GA)

  - Sucking (20 w GA)

  - Grasping hands, tiptoes, knees (22 w GA)

  - Opening mouth ***before*** hand to mouth/sucking (24 w GA)

    "***anticipatory mouth opening***"



Fetal anticipatory mouth opening ?

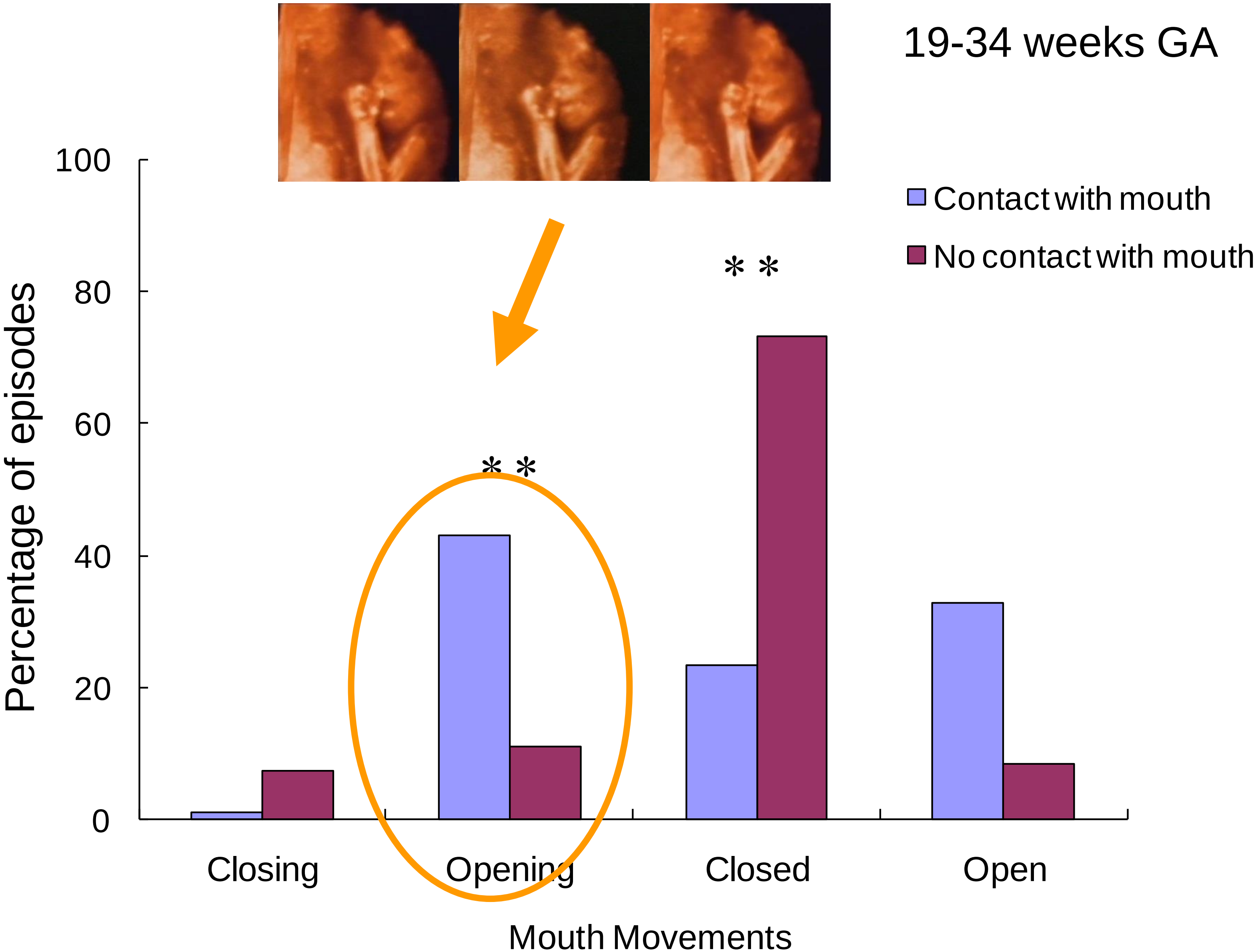
- Newborns show coordinated movements between their hands and mouths (**hand-to-mouth**)
- "**Anticipatory**" mouth opening before their hands come in contact with their mouths

Hand-Mouth contact is an action that reflects the anticipation of the goal, which is the behavioral evidence for "***intention***"

(primitive knowledge of ***self***)

Butter … chat, 2001

19-34 weeks GA



Myowa-Yamakoshi & Takeshita, 2007, *Infancy*

Development of proprioception in the womb

Myowa-Yamakoshi & Takeshita, 2007, *Infancy*

Fetuses learn mother’s voice

Human fetuses discriminate
mother’s voice
from other females’ voice

- Increase heart rate
- Responses were sustained for 4 min

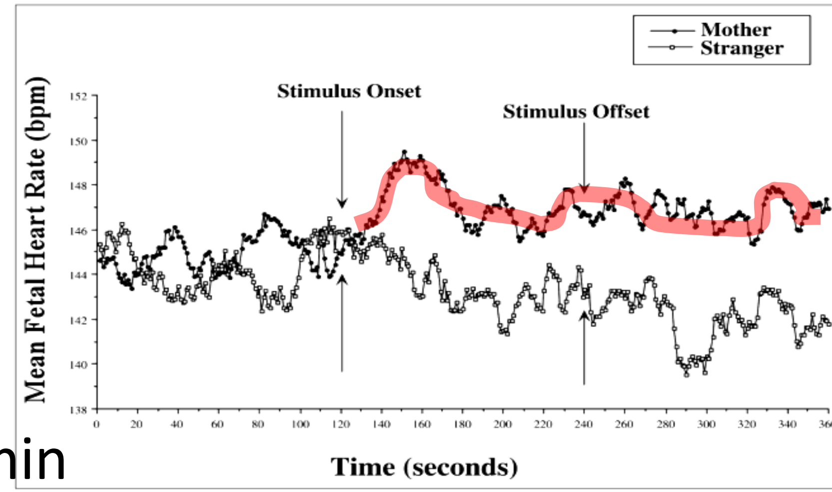
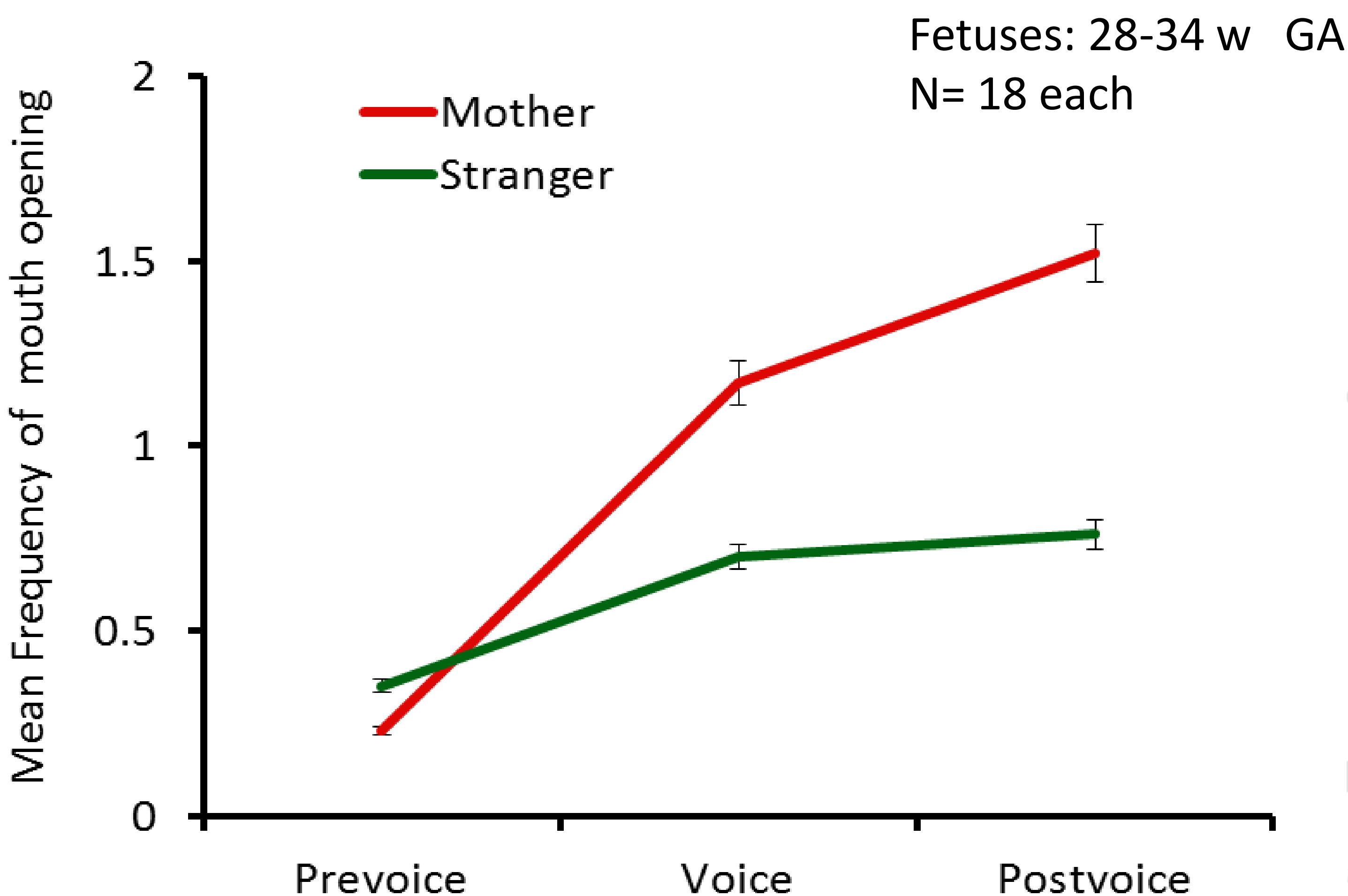


Fig. 1. Average fetal heart rate for the 2 min prior to voice onset, 2 min of mother’s or stranger’s voice, and 2 min following voice offset.

- **Activate oral movements !**

Kisilvsky et al., 2003, *Psy Sci*. Takeshita et al. 2012, *Interaction Studies*

Oral responses to mother's and stranger's voices



Takeshita et al. 2012, *Interaction Studies*, *Myowa-Yamakoshi et al., submitted*


narumiya maki
25w0d
MEDISON
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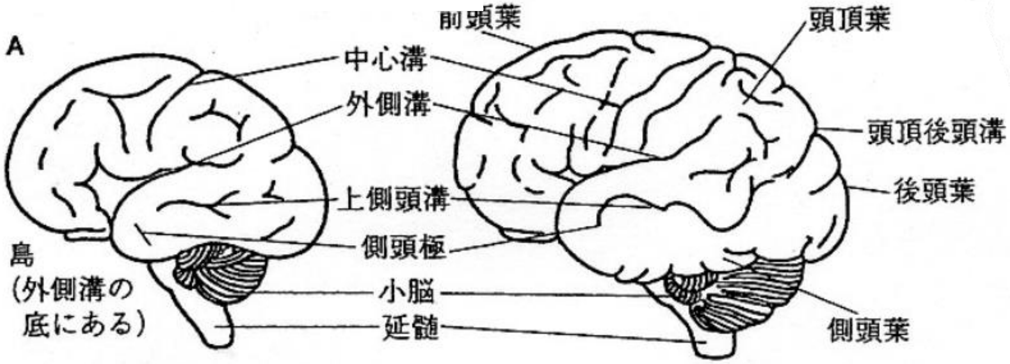
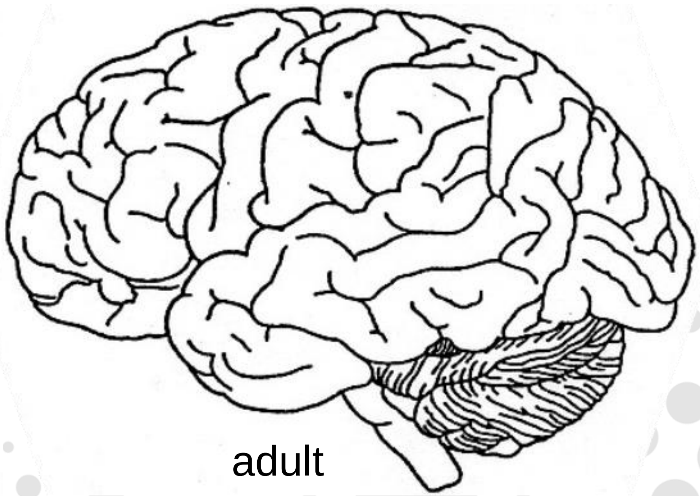
Fetal brain development in humans

4 month GA 6 month GA 7 month GA



8 month GA

9 month GA
（at birth）



adult

remarkable development in the last trimester of pregnancy

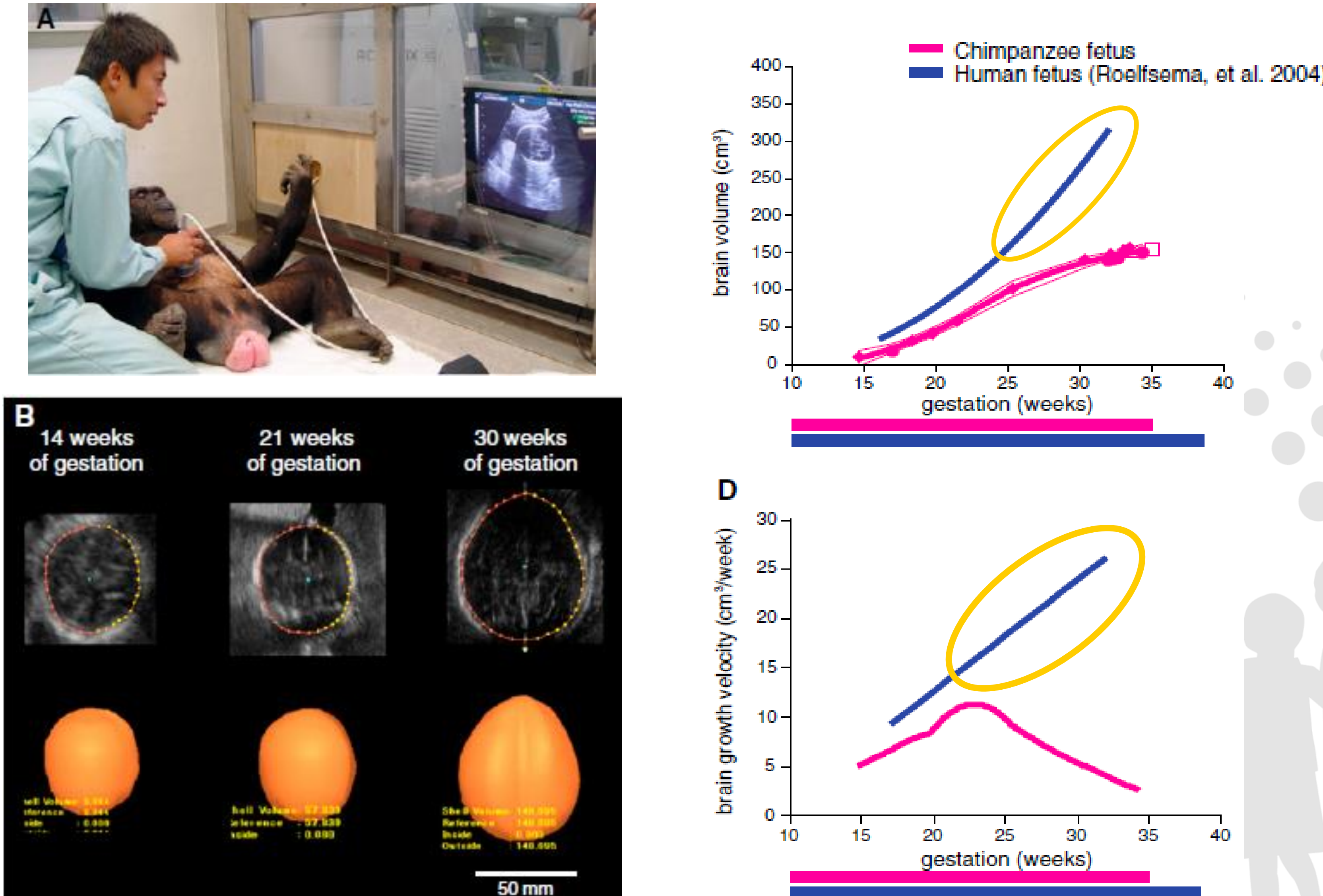
- increase in brain volume
- increase the amount of sulcal

Observation of chimpanzee fetuses

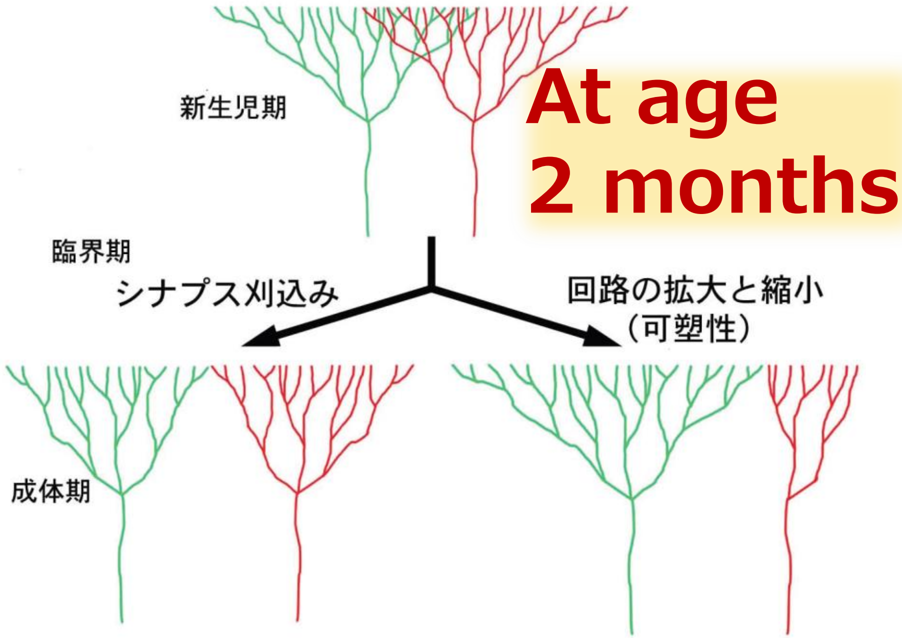
© Kyoto University

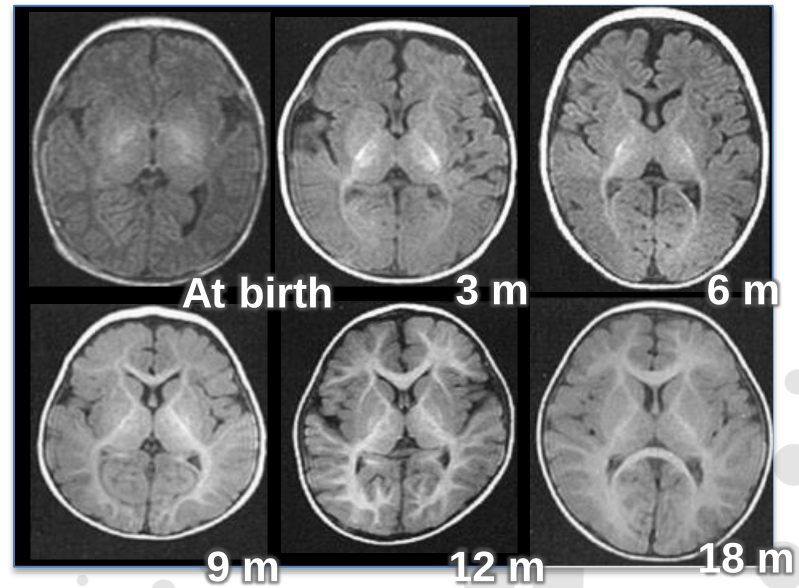
Remarkable enlargement of the human brain

Sakai et al., 2012, *Current Biology*



Development of early neural system





Myelination of axons

- **Explosion of synapse formation**
  densities peaking at age 2 months
  in all areas except visual area
- **Synaptic pruning**
  at different rates among different
  cortical areas (until teenage)

Effects of Postnatal Environment ?

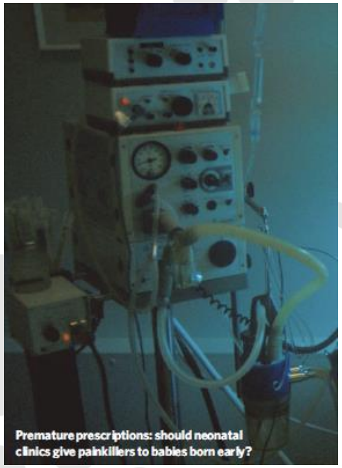
Development of Preterm Infants

Nature, 444(9), November 2006

Environment in NICU (neonatal intensive-care units)

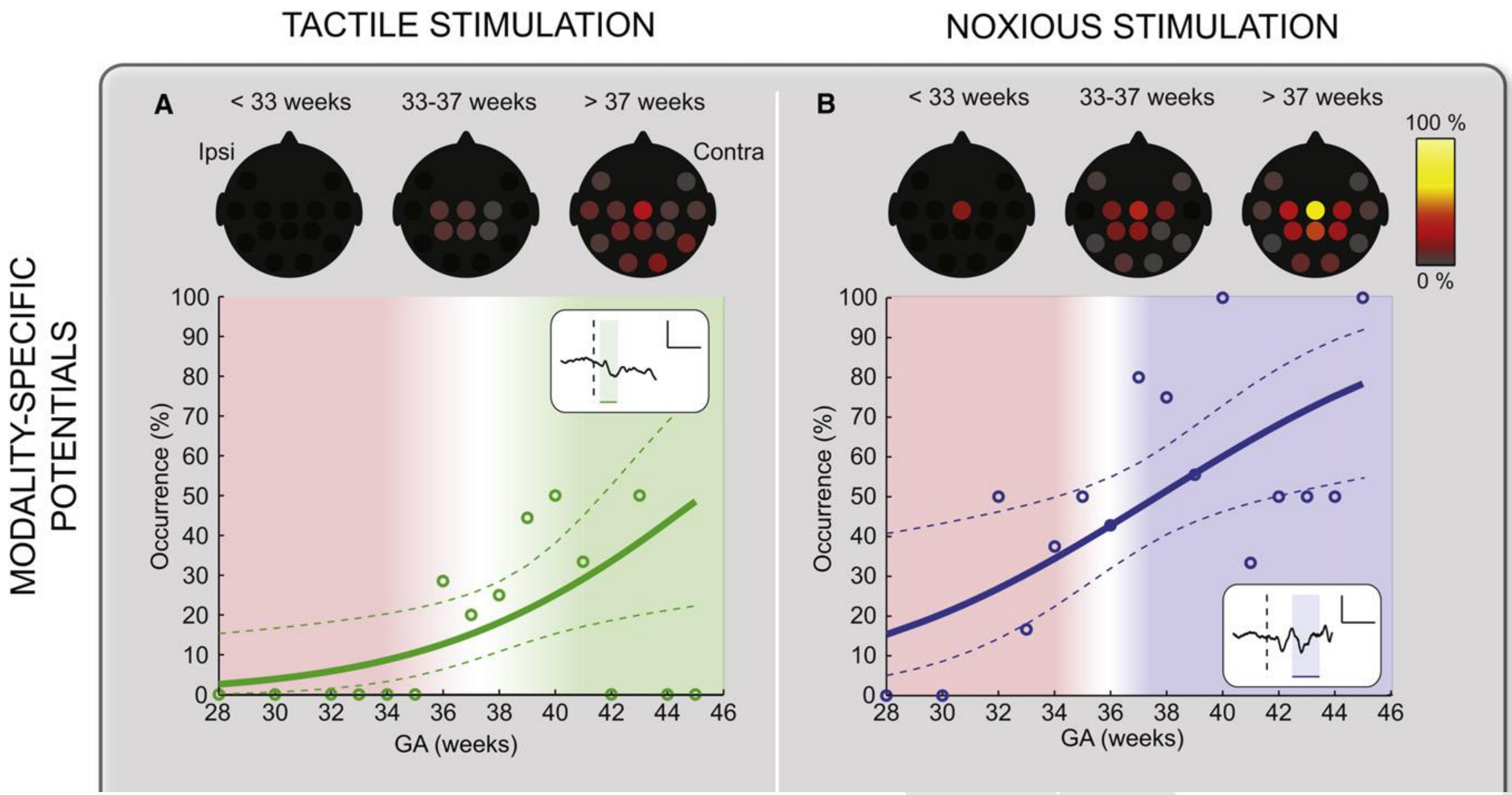
--- *Nature*, 444(9), November 2006

- excessive noise and light
- motionless in an incubator
- isolation from mother
- many routine medical procedures (may be painful)



A Shift in Sensory Processing that Enables the Developing Human Brain to Discriminate Touch from Pain

Fabrizi et al., *Current Biology*, 2011



- ✓ The human brain may discriminate touch from pain from 35–37 weeks GA
- ✓ **Before 35–37 weeks**, touch and noxious lance evoke nonspecific neuronal bursts
- ✓ **After 35–37 weeks**, touch and noxious lance evoke modality-specific potentials

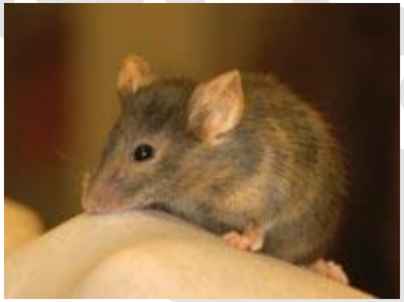
Preterm birth increases developmental risks

- Extremely preterm babies (<27 weeks of GA)
- Babies born **just two weeks early** are at higher risk of physical and mental problems than those born later

Lindstrom et al., 2011, *Pediatrics*

Higher risk of

- **Language development**
- **Cognitive** and **social-emotional** functioning
- **ADHD** (2.5 – 5 times greater)
- **LD** (4 – 6 times greater)
- **ASD** (5 times greater ?)



Nature, 2011

Long-term study of **gene–environment interactions** is needed

ANS assessment by infant cry

biology letters

rsbl.royalsocietypublishing.org

Research

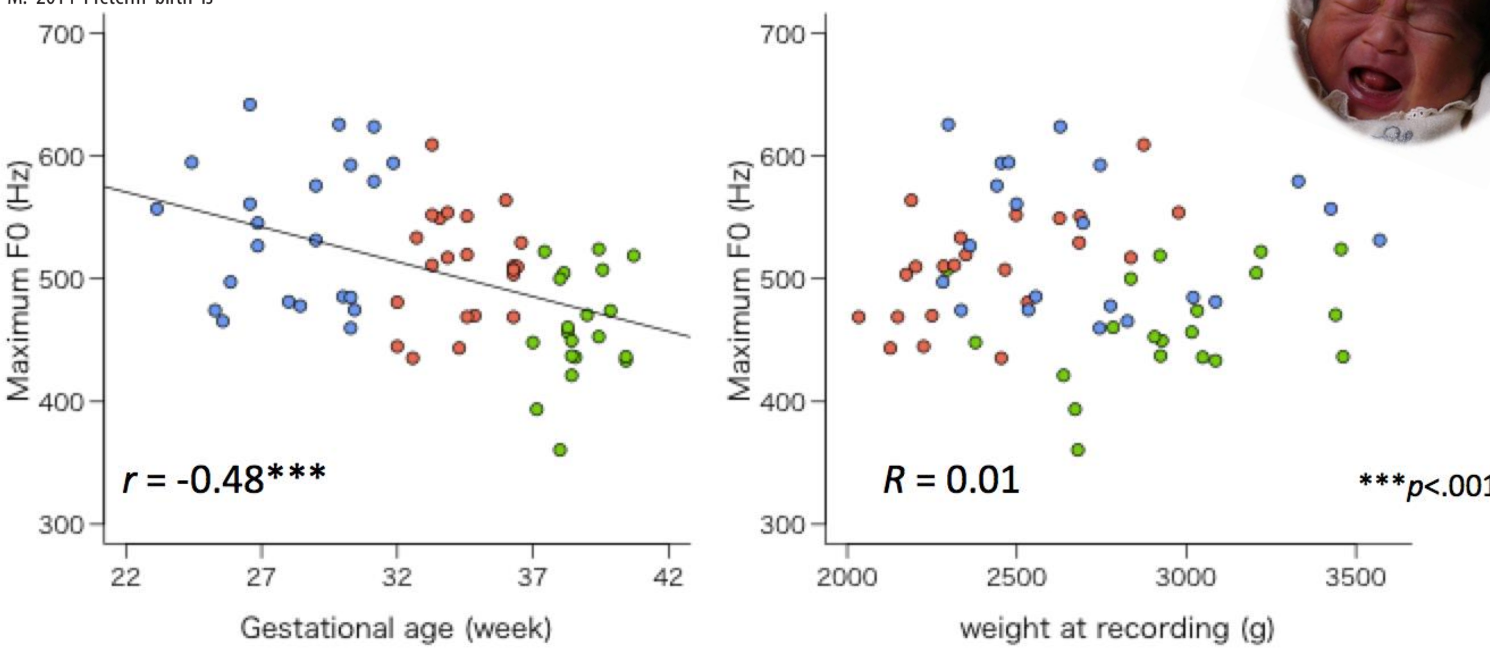
CrossMark
click for updates

Cite this article: Shinya Y, Kawai M, Niwa F, Myowa-Yamakoshi M. 2014 Preterm birth is

Animal behaviour

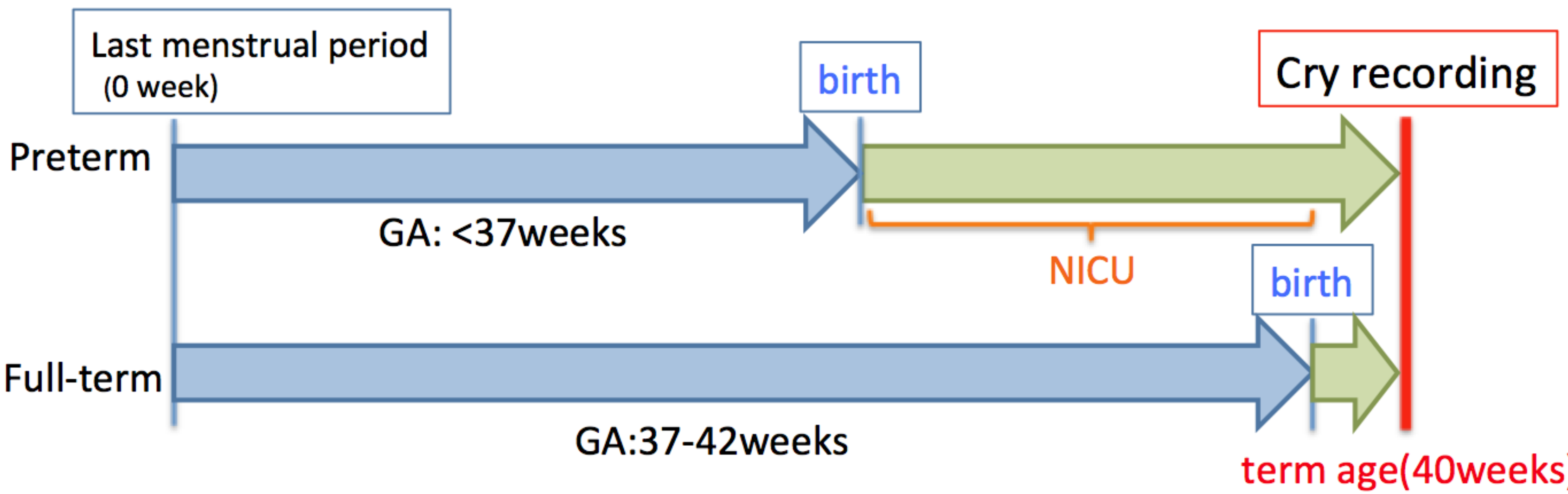
Preterm birth is associated with an increased fundamental frequency of spontaneous crying in human infants at term-equivalent age

Yuta Shinya[1,3], Masahiko Kawai[2], Fusako Niwa[2] and Masako Myowa-Yamakoshi[1]



Participants

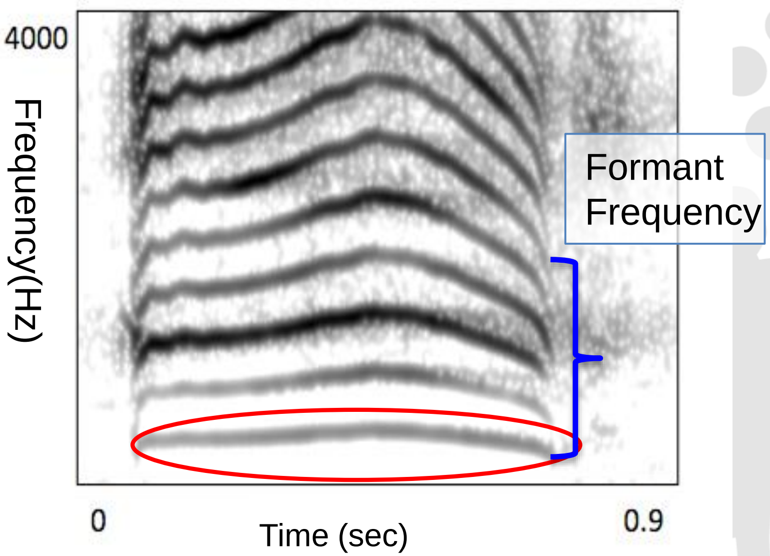
- ✓ Full-term newborns (n=20)
- ✓ Preterm infants of term-equivalent age (n=44)
  - ＊ They were born at Kyoto University hospital
  - ＊ No severe brain lesion and complications (e.g. IVH, PVL, cerebral palsy)



Recording and Analysis

- Spontaneous cries within 30 min before feeding
- Acoustic index:
  - Fundamental frequency (F0)
  - Duration
  - Formant frequency etc…

Investigation of the effects on infant cry
- **Gestational age**
- **Body size**
- **Intra Uterine Growth Retardation (IUGR)**



spectrogram of a cry utterance

Examples of infants' cry

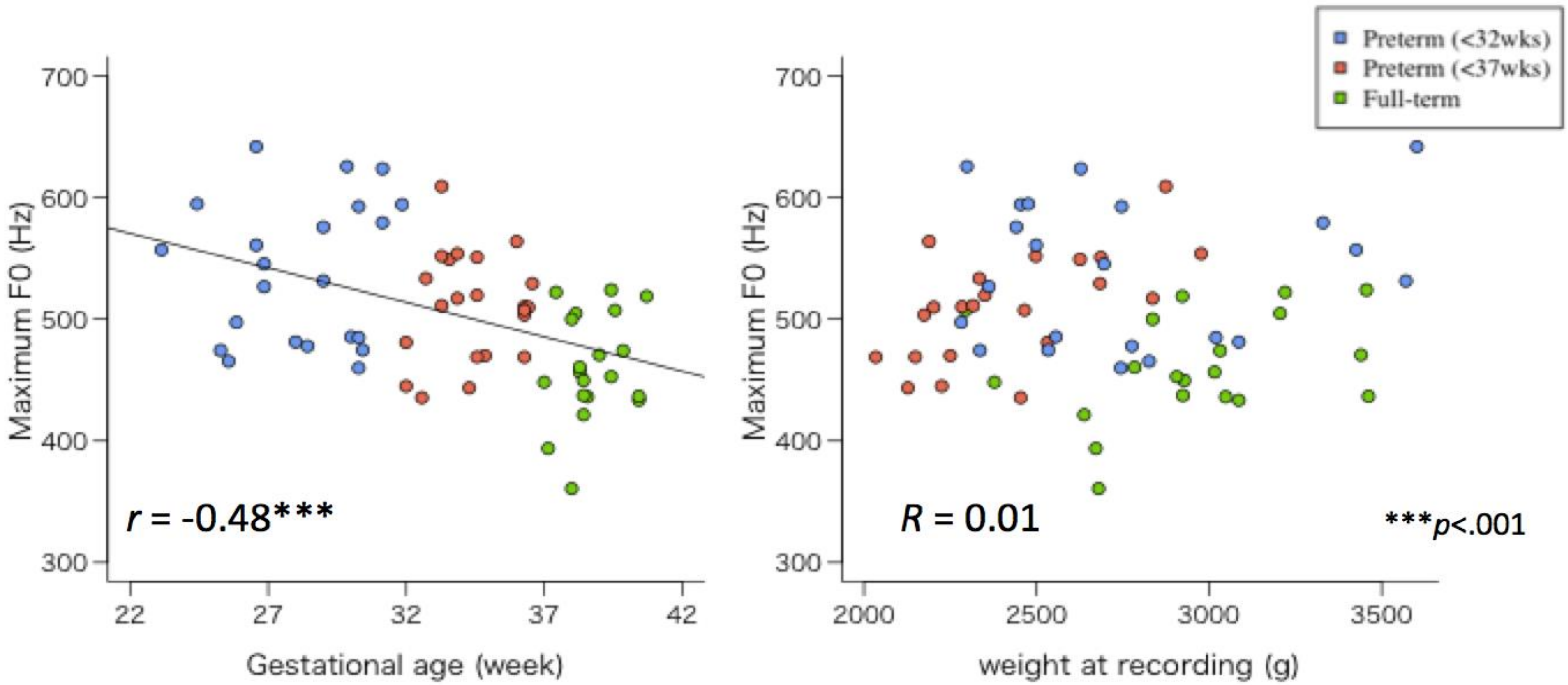
Full-term's cry

Preterm's cry

Results

1) Shorter gestational age is related to higher F0 of spontaneous cry at term-equivalent age

2) Higher F0 is not related to neither smaller body size nor IUGR

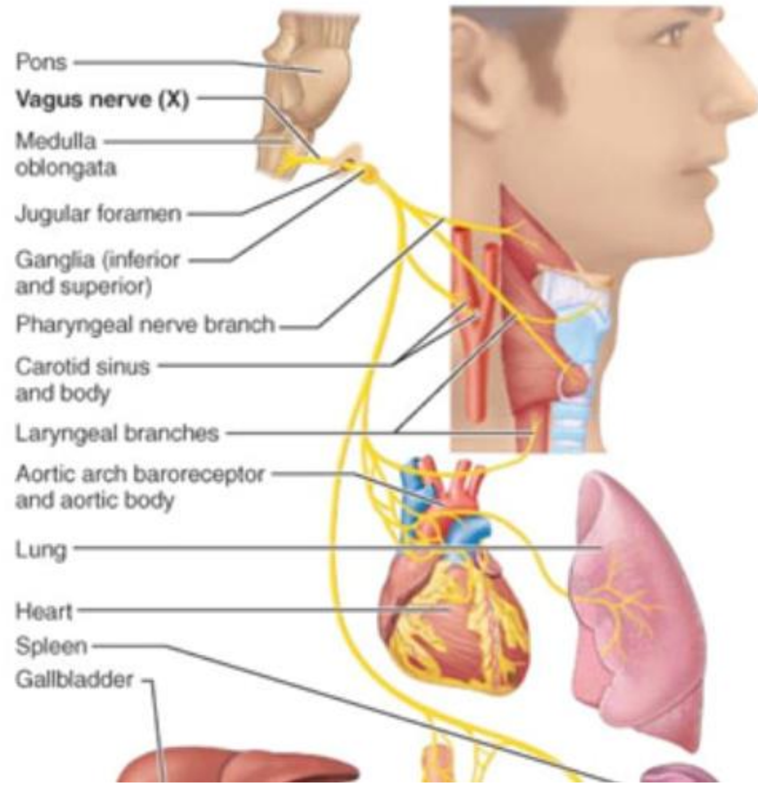


Why preterm birth increase F0 of spontaneous crying?

The effect of ***lower vagal activity*** on higher pitch of crying ?

Vagus nerve

- Parasympathetic nervous system
- Control of visceral organs
  (e.g. heart, larynx)
- Decrease tension of vocal folds
  (e.g. Patural et al., 2008)
- Preterms...
  lower vagal activity at term age relative to full-terms
  (e.g. Patural et al., 2008)



Data Analysis

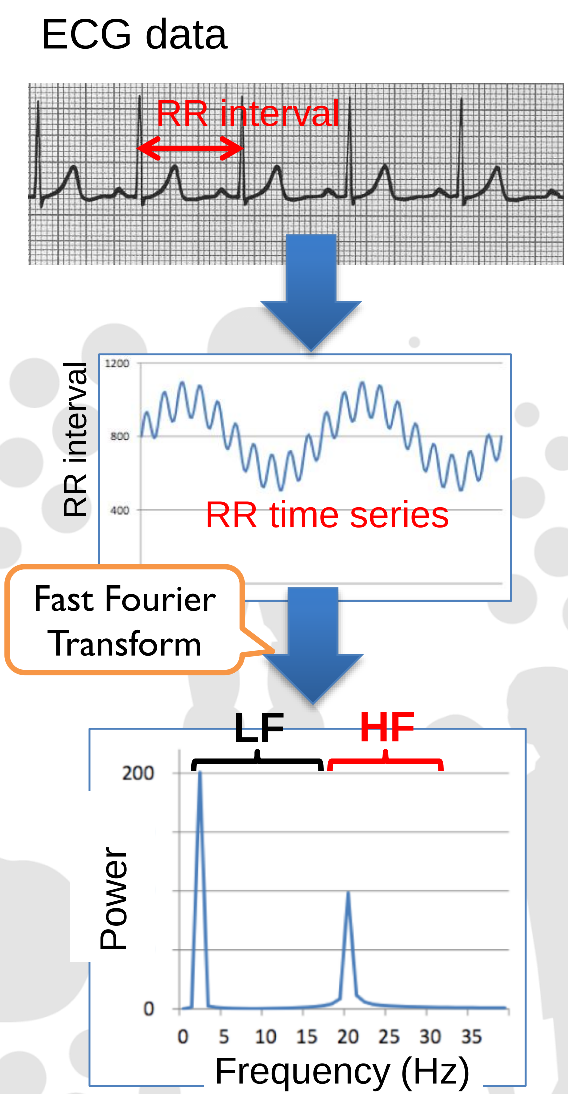
- ✓ Cry F0 × Vagal activity
- ✓ **Heart rate variability (HRV)**
  - RR intervals → RR time series
  - Spectra domain analysis using FFT

High freq component (**HF**: 0.25-1.50Hz)

- Respiration: **parasympathetic** (vagal activity)

Low freq component (**LF**: 0.04-0.24Hz)

- Blood pressure: sympathetic/parasympathetic

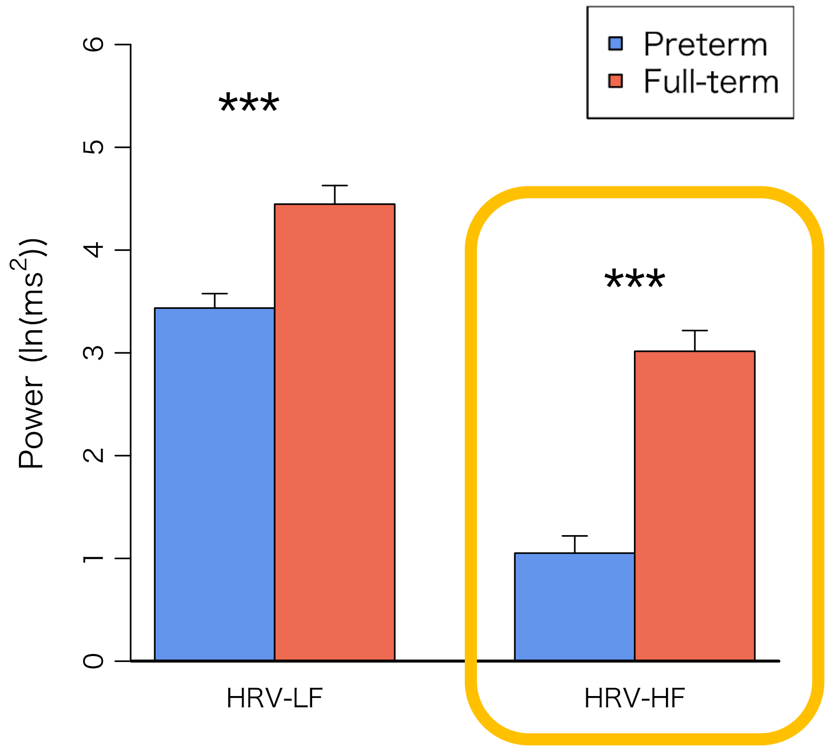


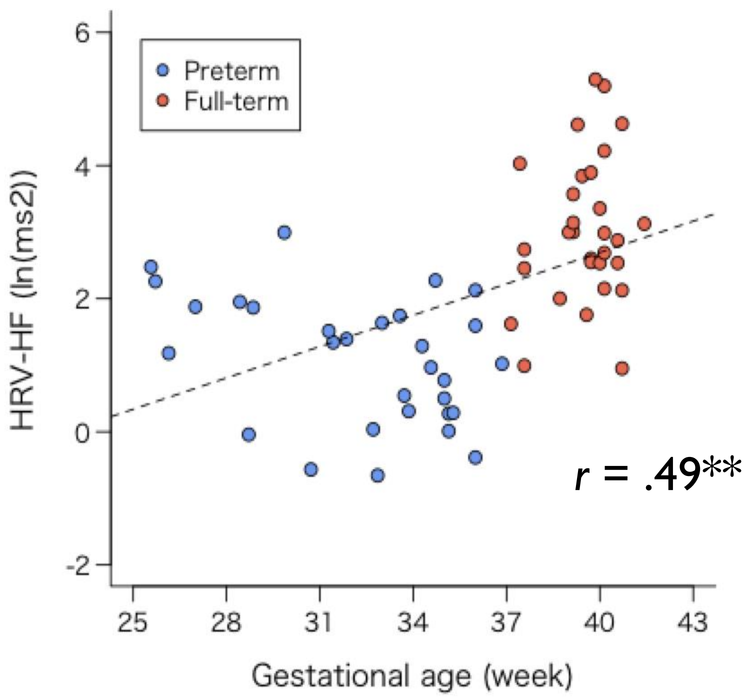
Resting Heart Rate Variability (HRV-HF)
HF component: parasympathetic nervous system

Preterms (n=30, 32.3GA), Full-terms (n=30, 39.5GA)

1) **HRV-HF**: ***Preterm < Full-term*** (t=5.59, p<.001)

2) **GA×HRV-HF**: ***Positive correlation*** (r=.49, p<.01)

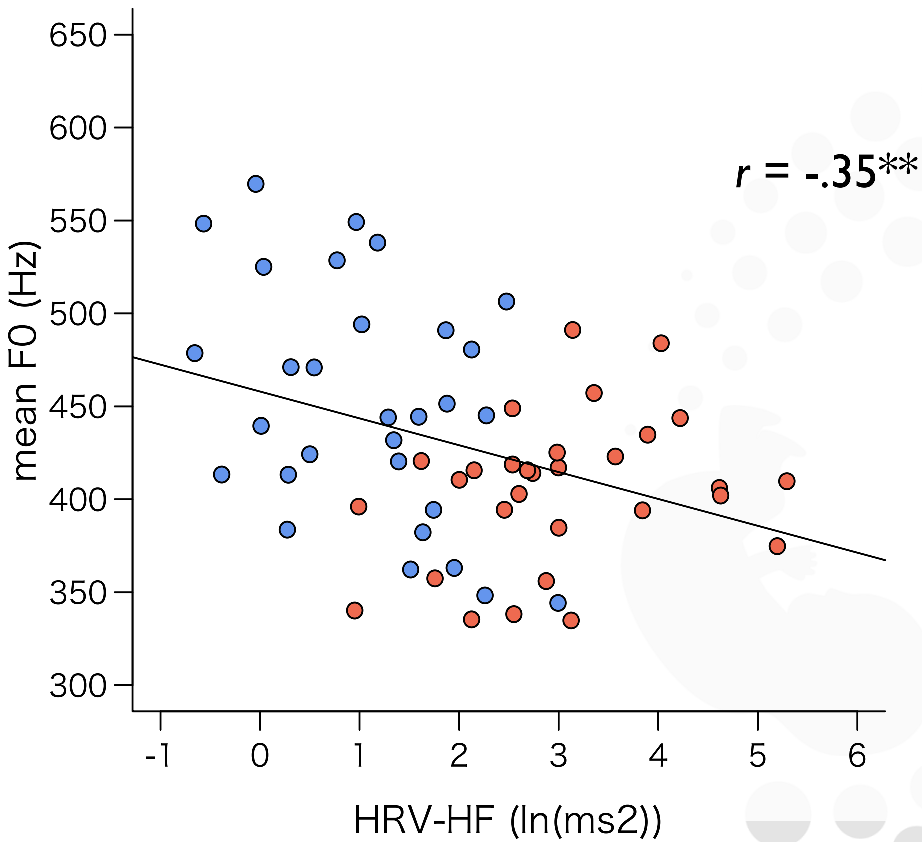




Resting HRV-HF × Cry F0

Resting HRV (HF) × F0 of spontaneous cry

→ **Negative correlation** （r=-.35, p <.01）



Science "Latest News"

Science
AAAS

12 Aug 2014

Premature baby's shrill cry may be sign of something deeper

Higher pitch could indicate lower activities in nerve that aids digestion

早産児ほど泣き声高く

京大グループ発表

予定日より早く生まれた赤ちゃんは、予定日前後に生まれた赤ちゃんに比べて高い声で泣く傾向があると、京都大のグループが19日、発表した。声の高低差には、心拍数を下げたり声帯の緊張を緩和したりする自律神経の一つ「迷走神経」の成熟や活動が関係しているとみている。

研究したのは、教育学研究科の明和政子教授や医学研究科の河井昌彦准教授、教育学研究科大学院生の新屋裕太さんらのグループ。

京大医学部付属病院で生まれた赤ちゃんのうち、妊娠から37～42週の満期児20人、32～36週と23～32週の早産児それぞれ22人について、全員が予定日前後まで成長した後の自発的な泣き声を調べた。その結果、満期産児は平均460ヘルツ、37～42週の赤ちゃんは同511ヘルツ、32～36週は同539ヘルツだった。

グループによると、泣き

迷走神経 成熟関与？

声の高低差に赤ちゃんの
重は関係していなかった
原因とみている迷走神
は、成人ではさまざまな
気との関連が分かってい
という。

明和教授は「早産児で
声が低かったり、逆に満
児でも声が高かったりする

早産の赤ちゃん 高い泣き声

京大グループ解明 神経の働き影響か

早産の赤ちゃんほど、高い声で泣く――。京都大の明和政子教授（発達科学）らのグループは19日、こんな研究成果を発表した。神経が十分働いていないことが影響している可能性があり、今後、発育などとの関連を追跡調査する。

成果は英科学誌バイオロジー・レターズ電子版に掲載された。早産の赤ちゃんの泣き声が高いことは以前から知られていたが、詳細は不明だった。

明和さんらは、京大付属病院で生まれた赤ちゃん計64人について、妊娠40週前後に当たる時点の泣き声を分析した。妊娠37週以上で生まれた赤ちゃんの泣き声の高さは平均460ヘルツ。早産とされる37週未満では、36～32週が511ヘルツ、32週未満では539ヘルツだった。ただ、個人差が大きく、37週以上の平均値よりも泣き声が低い早産の赤ちゃんもいた。体の大きさや母親の胎内での発育状況に関連はみられなかった。

早産の赤ちゃんは喉頭（こうとう）や心臓などの調整に関わる「迷走神経」の働きが低いという報告があり、のどの筋肉をうまく調節できずに泣き声が高くなっている可能性があるという。（阿部彰芳）

早産の赤ちゃん 高い泣き声

京大 自律神経の活動に関係か

京都大大学院教育学研究科の明和政子教授らの研究グループが19日、「早い時期に生まれる赤ちゃんほど高い声で泣くことが分かった」と発表した。研究グループは泣き声の高さは自律神経系の活動の度合いと関連している可能性があるとし、早産児の発達の仕組みを知る手がかりになりそうだ。論文は12日に英科学誌のオンライン版に掲載された。

研究グループは早産（在胎32週未満と32～36週）と満期産（37～42週）の赤ちゃん計64人の空腹時の泣き声を録音して解析。その結果、32週未満の周波数は460～642ヘルツ▽32～36週は435～609ヘルツ▽満期産は361～524ヘルツで、早く出生した子ほど周波数が高く泣き声が高い傾向があった。体の大きさとの関連はなかったという。

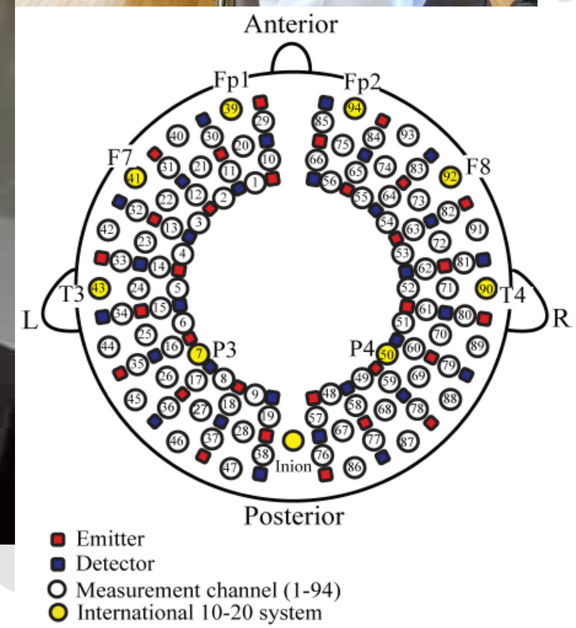
これまでの研究で、生後間もない早産児は自律神経系の一つである迷走神経の活動が低いことが報告されている。迷走神経は喉の緊張を和らげる働きがあり、研究グループは高い声は声帯の過度な緊張と関連しているとみている。

明和教授は「早産児は迷走神経の活動が未熟であることが、声の高さによって改めて示された。長期的な神経の発達とどのように関連するのか慎重かつ継続的に観察したい」と話している。【野口由紀】

SHANNON DRAWE/ISTOCKPHOTO/THINKSTOCK

Preterm infants at term-equivalent age vs. full-term newborns

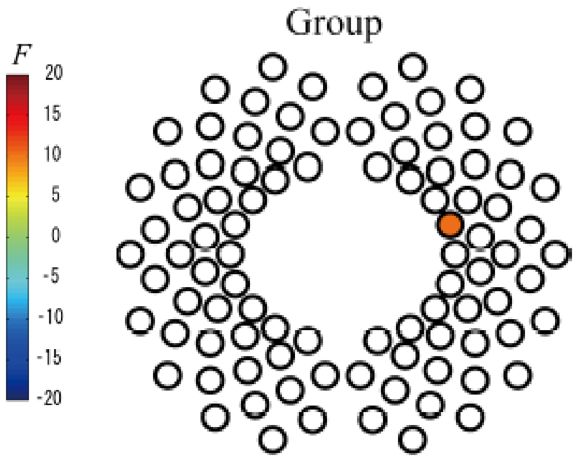
- Cortical activation in response to speech stimuli
- 94-channel Near-infrared spectroscopy (NIRS)



Preterm infants at term-equivalent age and Full-terms show different speech processing

Activation (oxy-Hb)

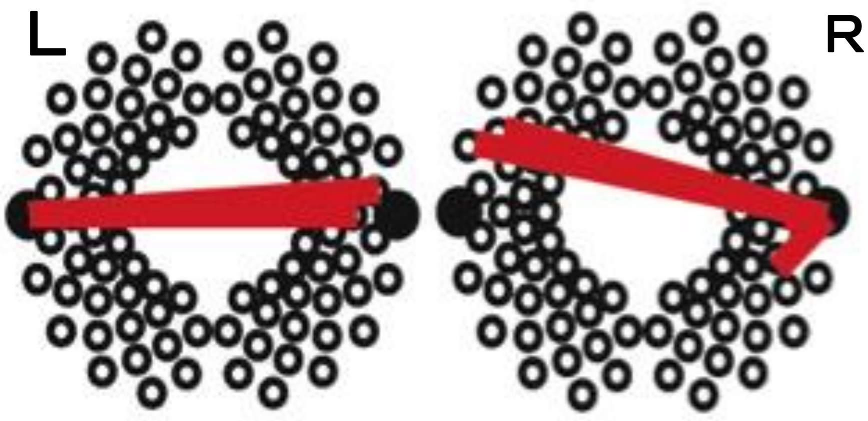
Full-term > Preterm



lower right temporal activation

Functional Connectivity

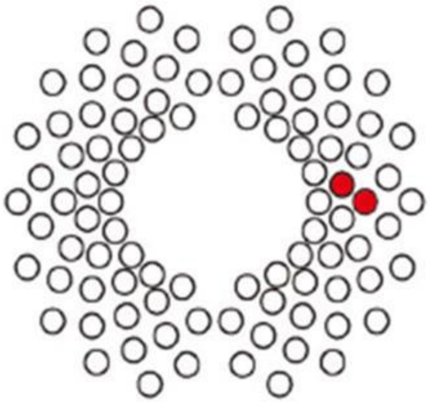
Preterm > Full-term

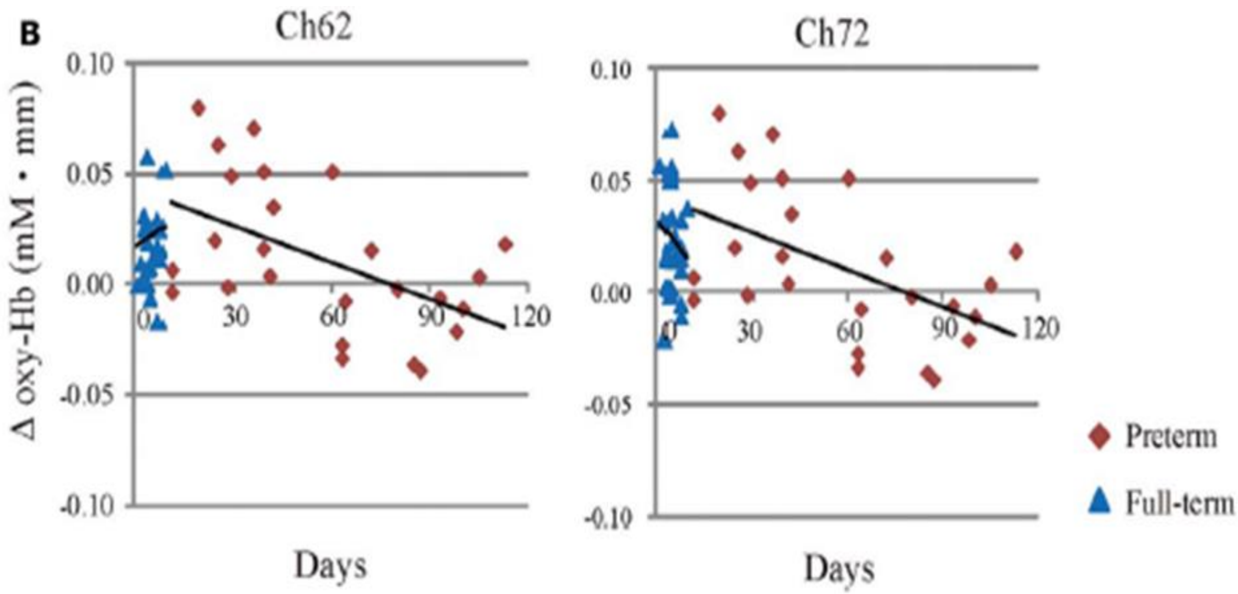


higher interhemispheric connectivity

Naoi et al. (2013)

Cerebral responses were inversely correlated with PNA in the right temporal region of the preterm infants





The channels with significant correlations between the PNA and oxy-Hb changes

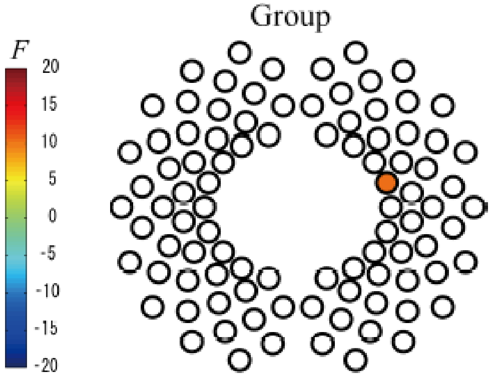
Oxy-Hb changes were **inversely correlated** with PNA in Ch62 and Ch72 in **the right temporal region** of the preterm group

Naoi et al. (2013)

Preterm infants at term-equivalent age and Full-terms show different speech processing

Activation (oxy-Hb)

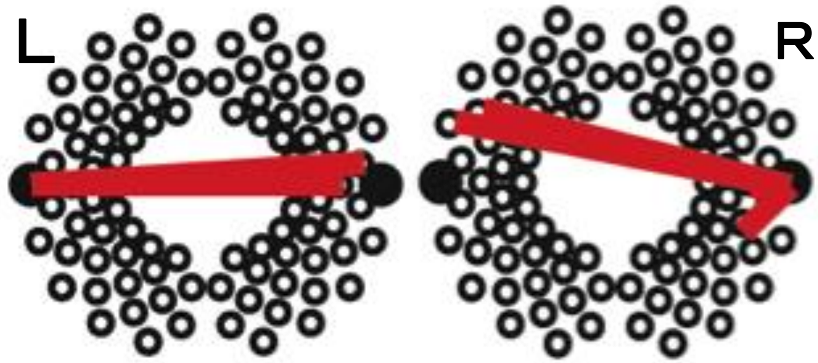
Full-term > Preterm



lower right temporal activation

Functional Connectivity

Preterm > Full-term



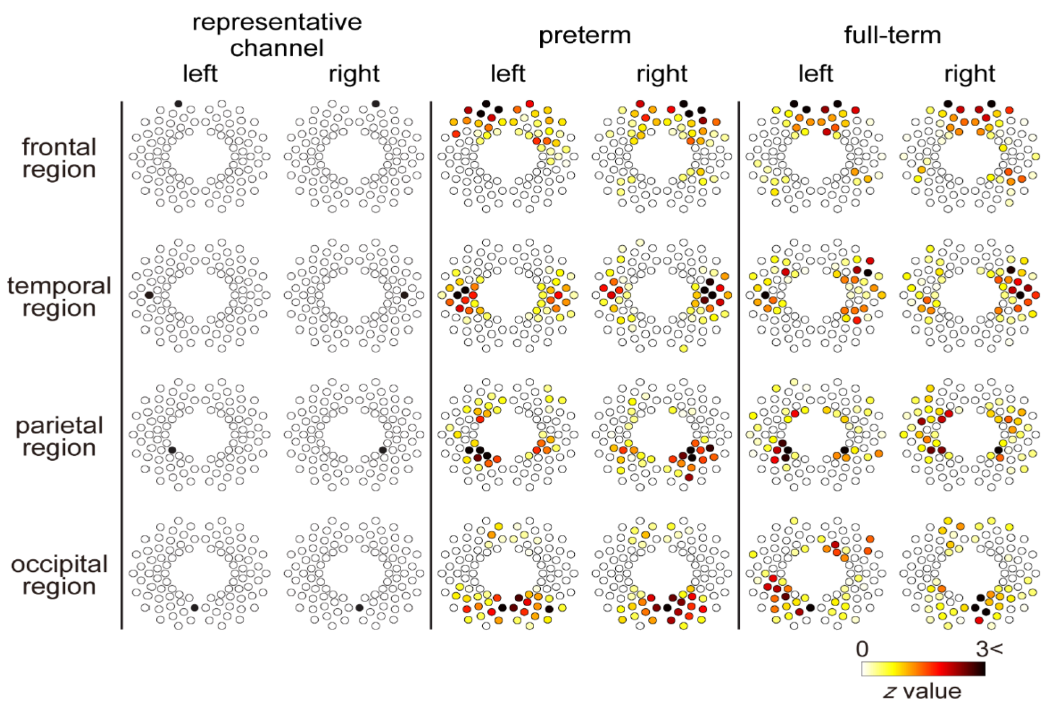
higher interhemispheric connectivity

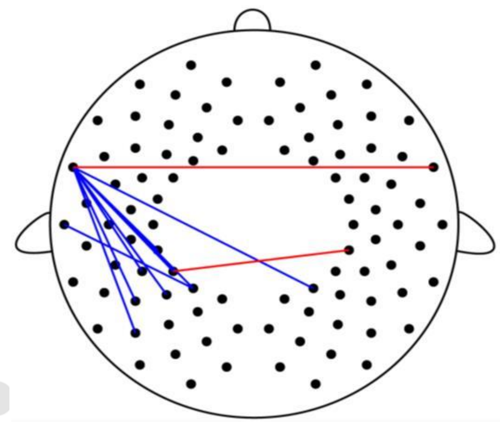
Preterm infants follow developmental trajectories different from those born term ?

Naoi et al. (2013)

Resting-State Functional Connectivity (RSFC)

Fuchino et al. (2013)





Red: the connections higher in **preterm infants**

Blue: the connectio higher in **full-term r ates**

later cognitive language development?

Preterm infants and full t t developmental trajector e

- RSFC between the **bilateral te p**
  preterms > full-terms
- RSFC between the **left temporal and left parietal** regions
  full-terms > preterms

Follow-up study on preterm infants’ development

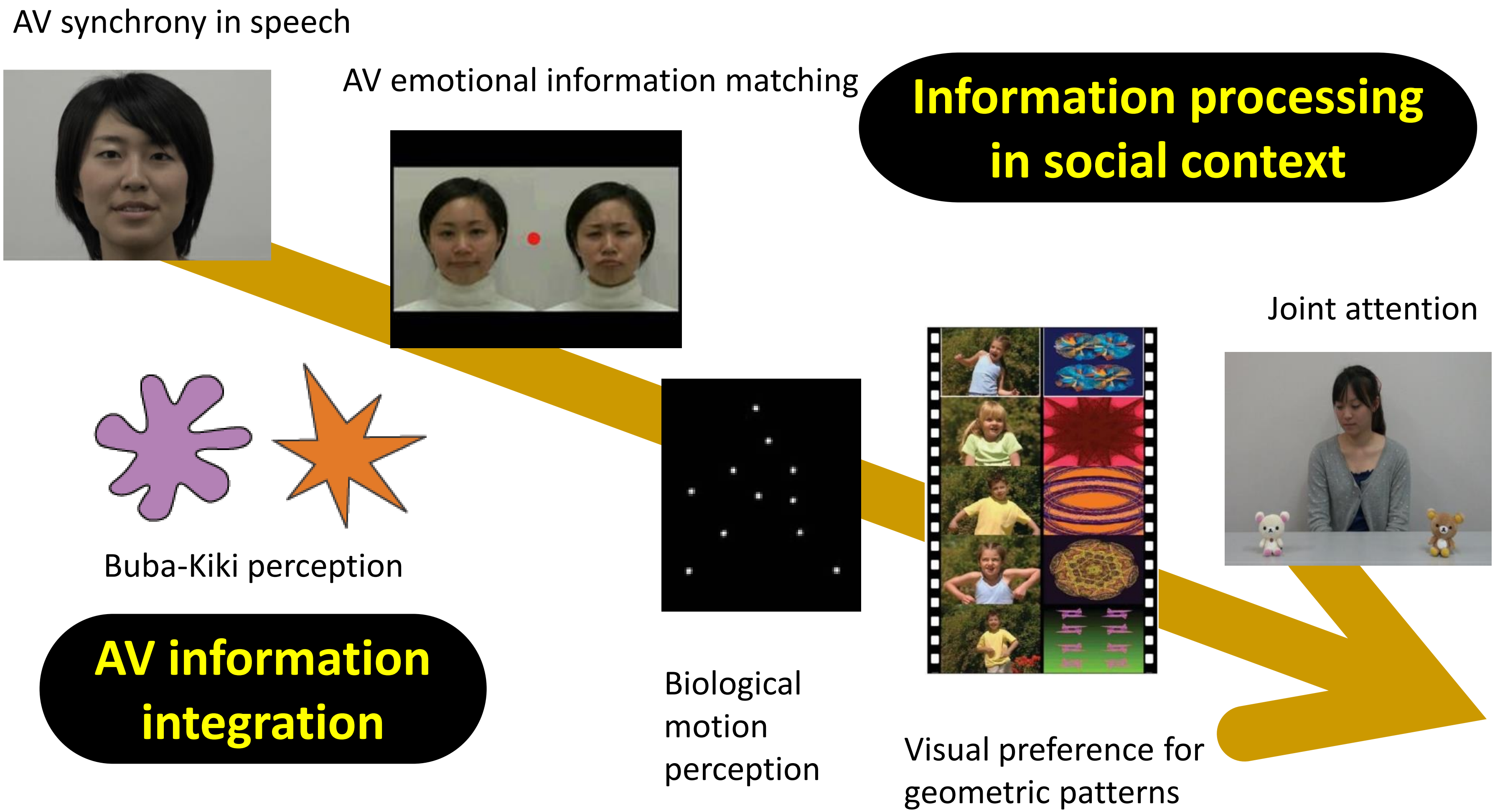
- Follow-up during the first two years of life
- Comparison of attention patterns between preterms and full-terms

(1) Audio-Visual integration processing

- Sensitivity for A-V synchrony
- Buba-Kiki perception
- A-V emotional information matching

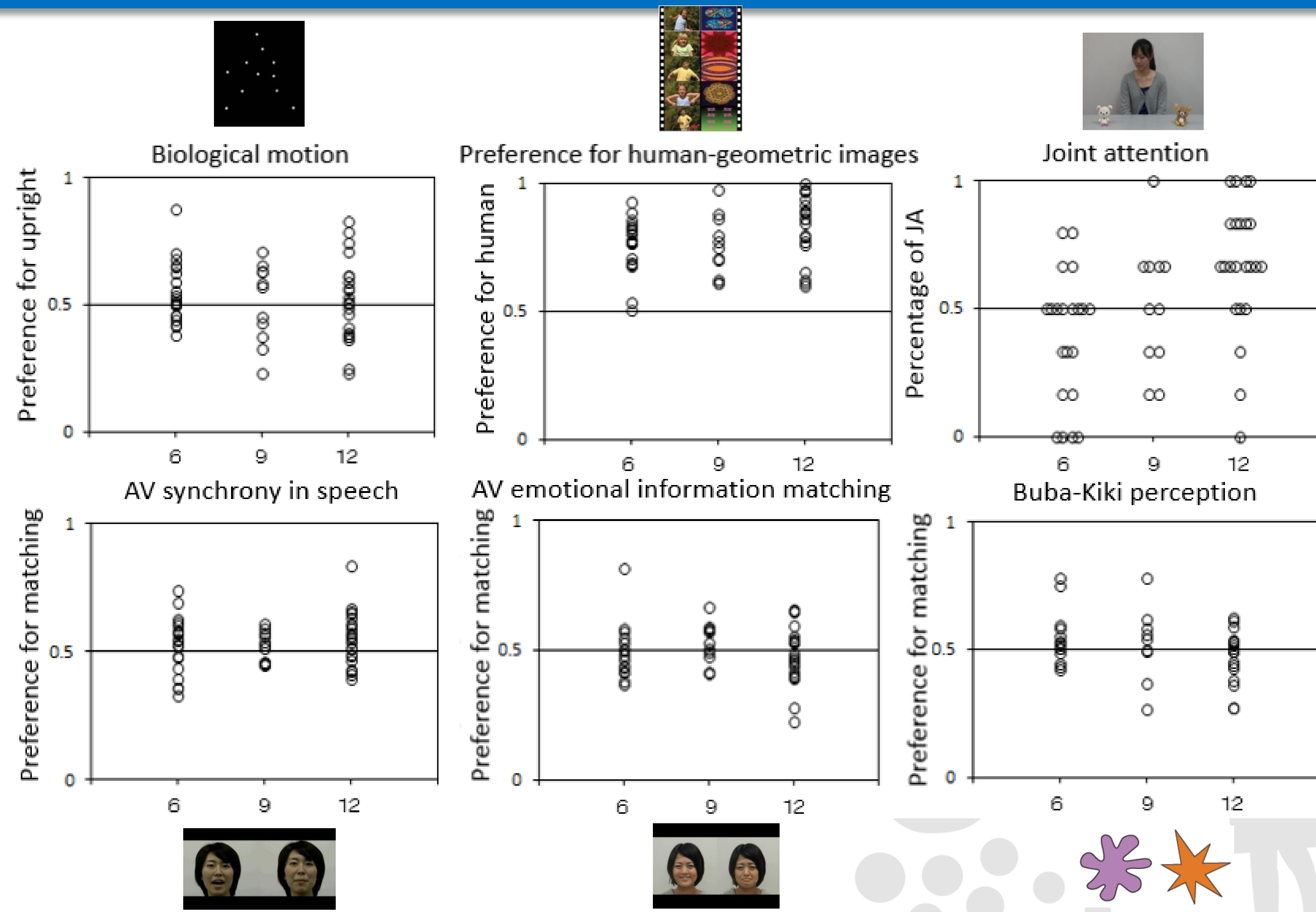
(2) Attention to social stimuli

- Biological motion perception
- Visual preference for geometric patterns and humans
- Joint attention

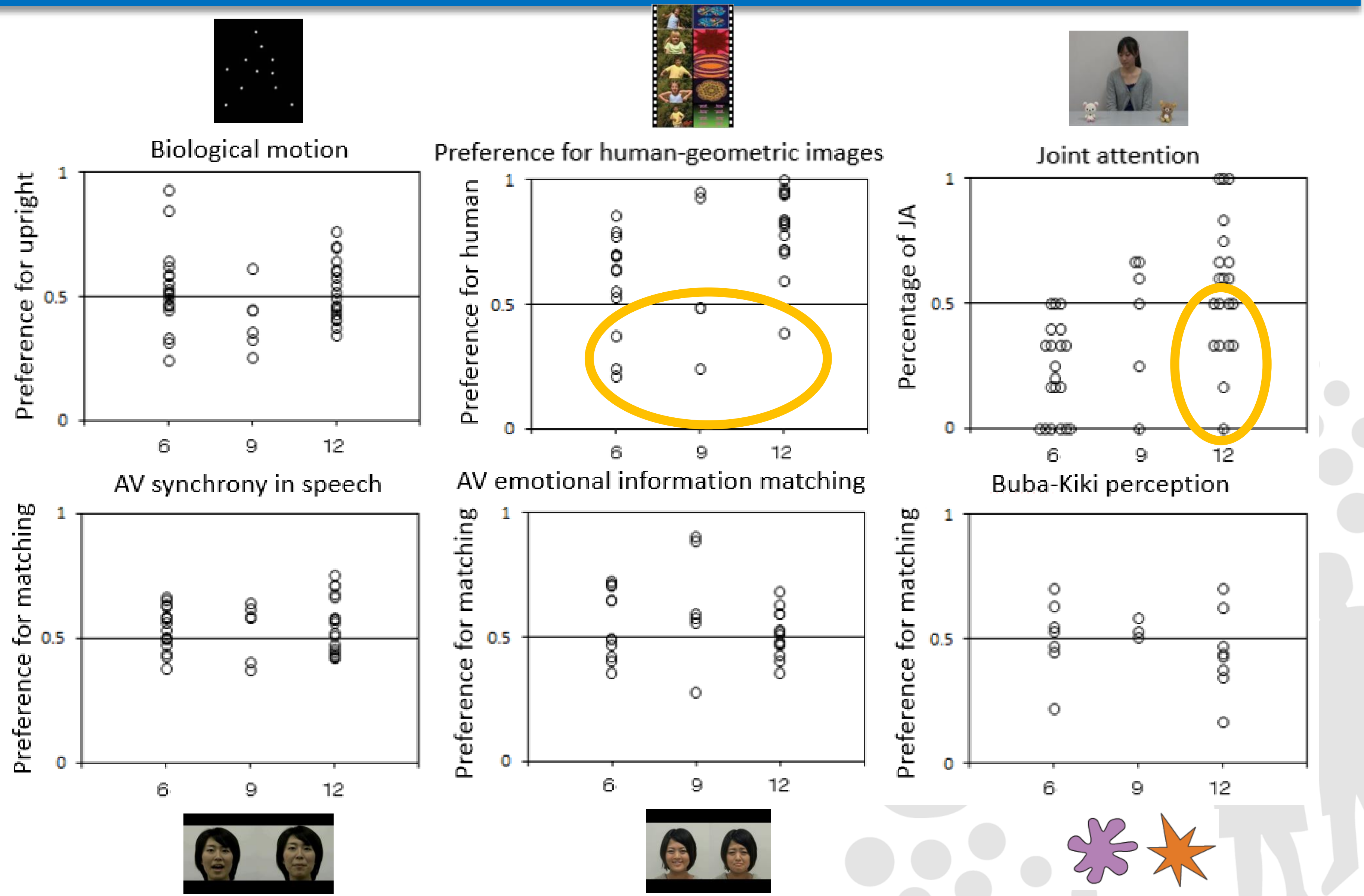


8~10 min at maximum

Full terms (n=55)

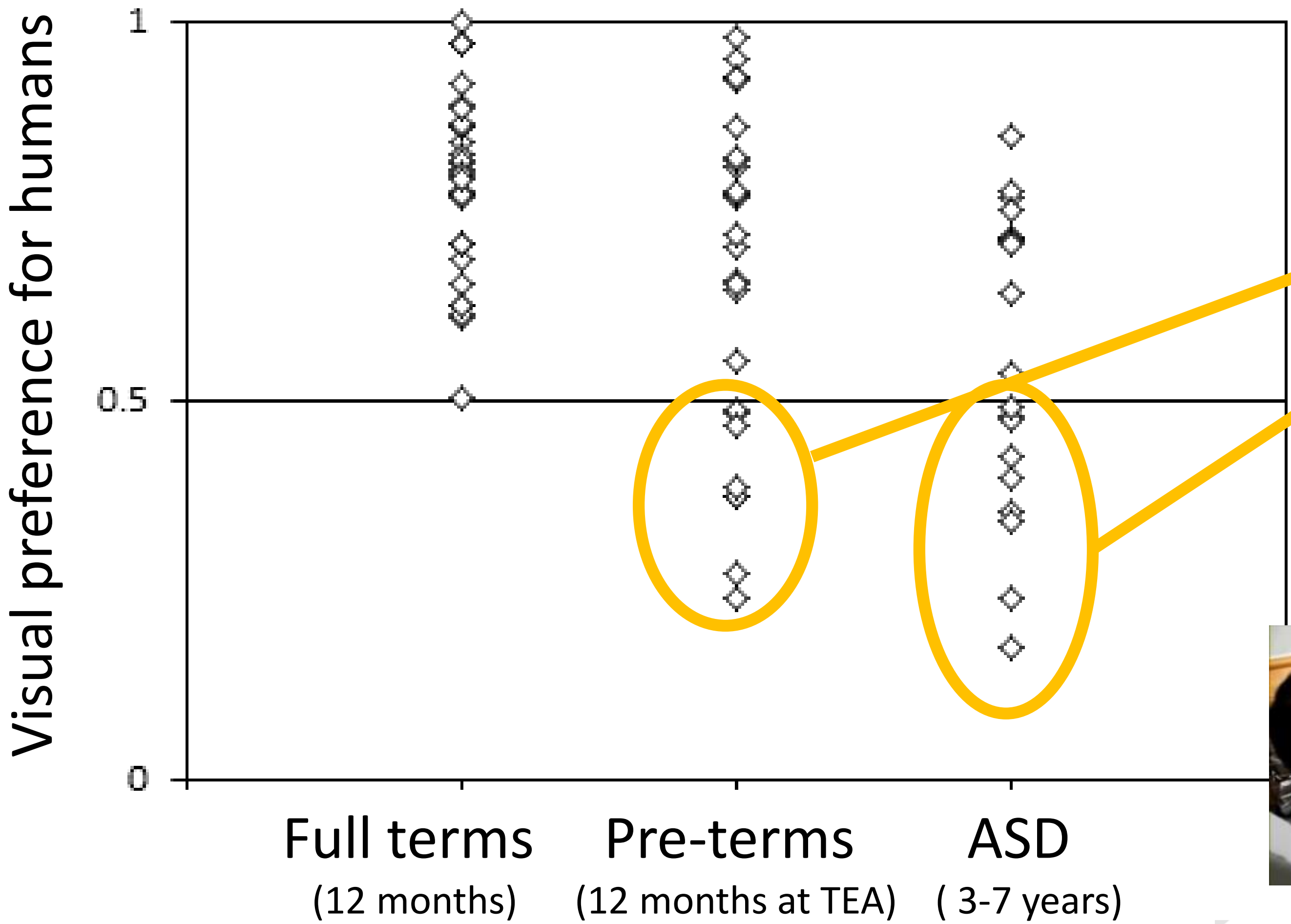


Preterms at term-equivalent age (n=56)



Preference for geometric patterns

Preference over 60% for geometric patterns is early predictive diagnosis biomarkers for ASD (Pierce et al., 2011)



Joint research with Dr. Umino (Aoyama Clinic, Tokyo)

Impairment of Motor Control in ASD

doi:10.1093/brain/awt208 Brain 2013: 136; 2816–2824 | 2816

BRAIN
A JOURNAL OF NEUROLOGY

Atypical basic movement kinematics in autism spectrum conditions

Jennifer L. Cook,[1,2] Sarah-Jayne Blakemore[1] and Clare Press[3]

Individuals with autism spectrum conditions have difficulties in understanding and responding appropriately to others. Additionally, they demonstrate impaired perception of biological
whether individuals with autism move with an atypical kinema
impairments, and in principle may contribute to some of their
acceleration and jerk while adult participants with autism and
movements. Additionally, participants with autism took part in
observed movements as 'natural' or 'unnatural'. Results show tha
did not minimize jerk to the same extent as the matched typical c
The degree to which kinematics were atypical was correlated wit
with the severity of autism symptoms as measured by the Auti
mental differences in movement kinematics in autism might he
developmental experience of their own atypical kinematic profil

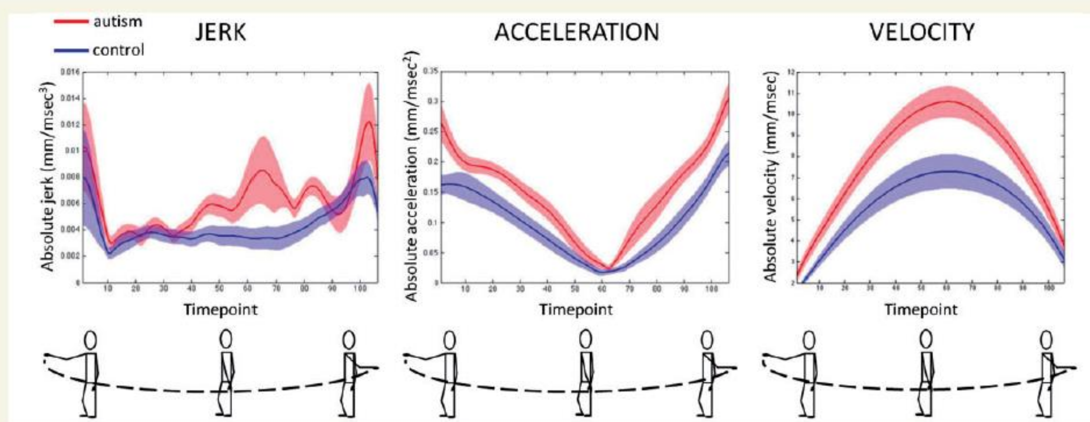
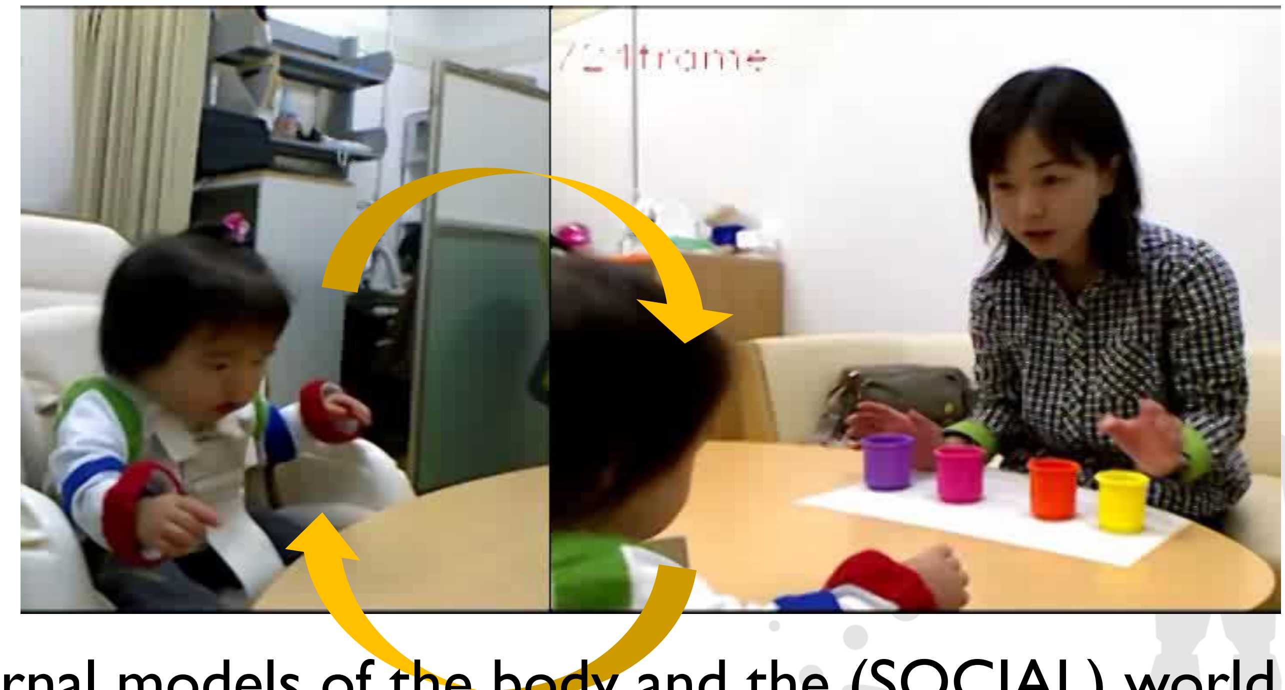


Figure 3 Basic kinematics of arm movements for control participants and individuals with autism in the primary task. When executing simple sinusoidal arm movements individuals with autism made more jerky movements (*left*) and travelled with faster absolute acceleration (*middle*) and velocity (*right*). Mean movement vectors are plotted in red for the autism group and blue for the control group. Shaded regions indicate the standard error of the mean.

Motor control and Social cognition



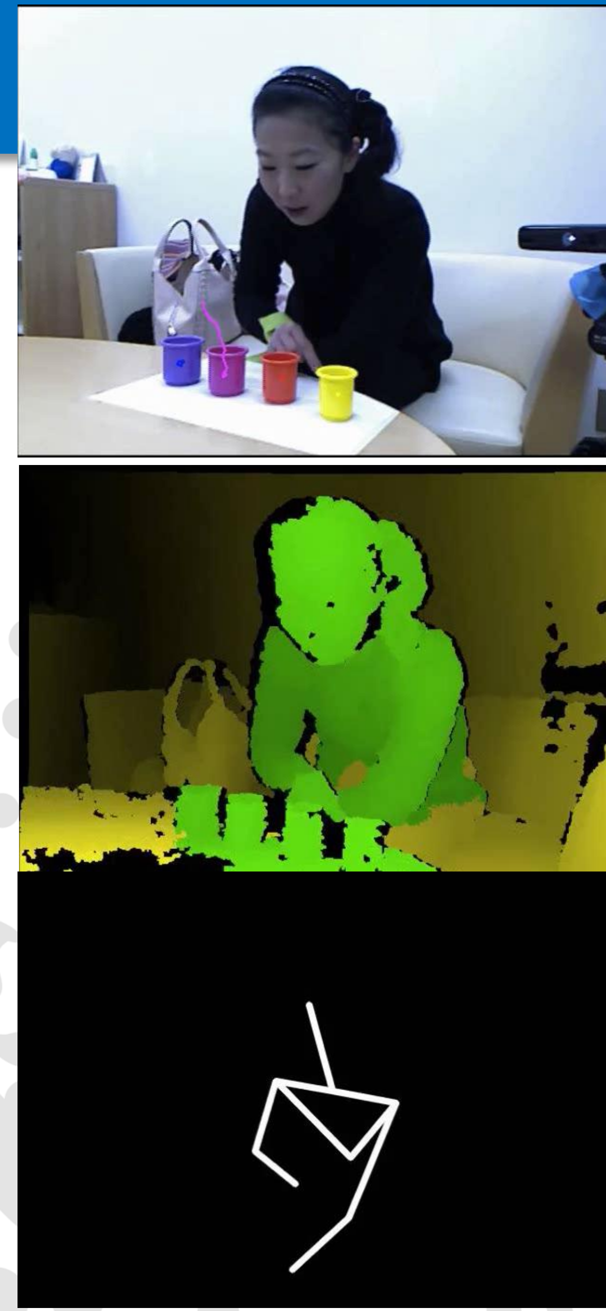
" Internal models of the body and the (SOCIAL) world "

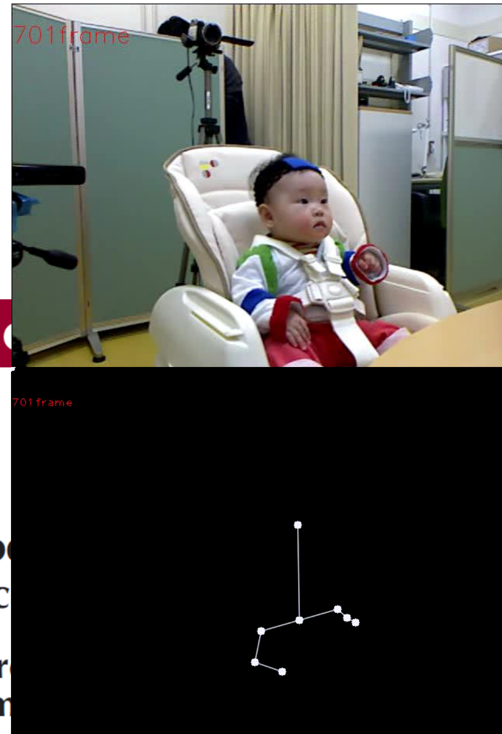
Motor control in Social Context:

- Sensori / Motor Prediction / Feedback
- Error correction
- Estimation of Motor commands

How Motor Control System relates to Social Cognitive Development?

Motion Capture





Developmental Scienc

Developmental Science (2014), pp 1–8

SHORT REPORT

Infant's action skill dynamically mo demonstration in the dyadic interac

Hiroshi Fukuyama,[1] Shibo Qin,[2] Yasuhir Minoru Asada[2] and Masako Myowa-Yam

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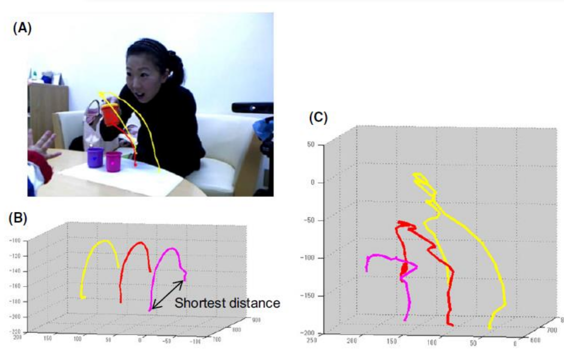
2. *Graduate School of Engineering, Osaka University, Japan*

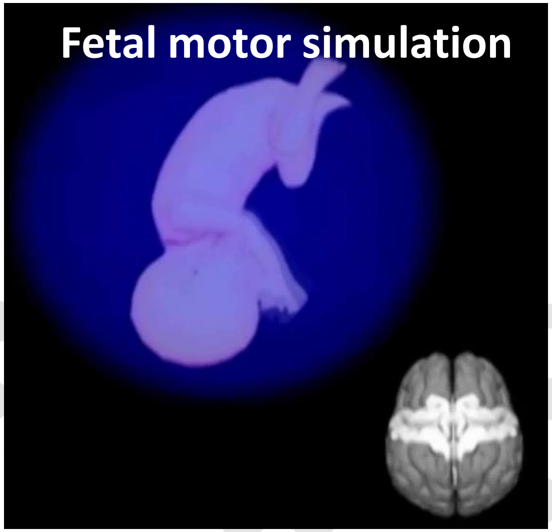


Abstract

When interacting with infants, human adults modify their demonstrated that infant-directed modification affects the directed modification is elicited during infant–parent intera affects the mother's action during an interaction. We rec mothers demonstrated a cup-nesting task during interactio that spatial characteristics of the mother's task demo manipulation. In particular, the variance in the distance th

New approach: *Constructive Developmental Science*

- ***"Constructive Developmental Science"***
- Understanding
  the **principles of human development**
  by analyzing data and modeling it
  from the perinatal period
- **New understanding of human mind and its disorders**



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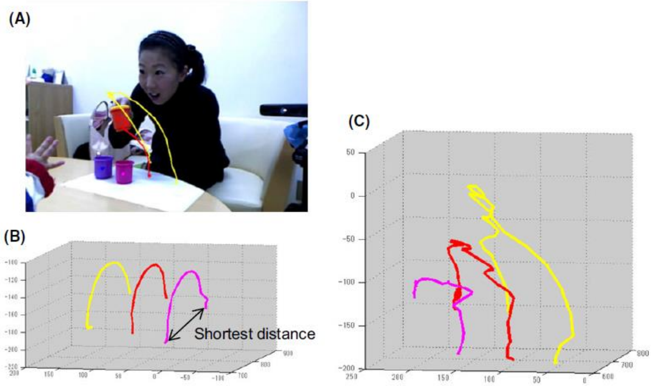

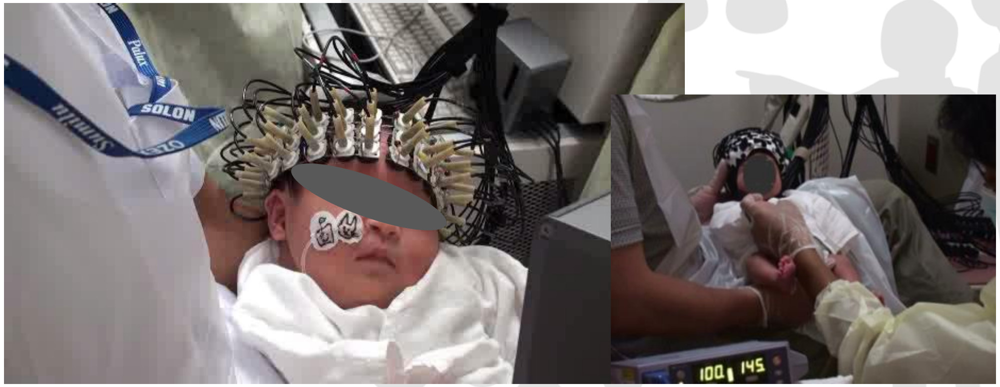

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