

Inhibitory Processes in Childhood Development and Aging

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OVERVIEW

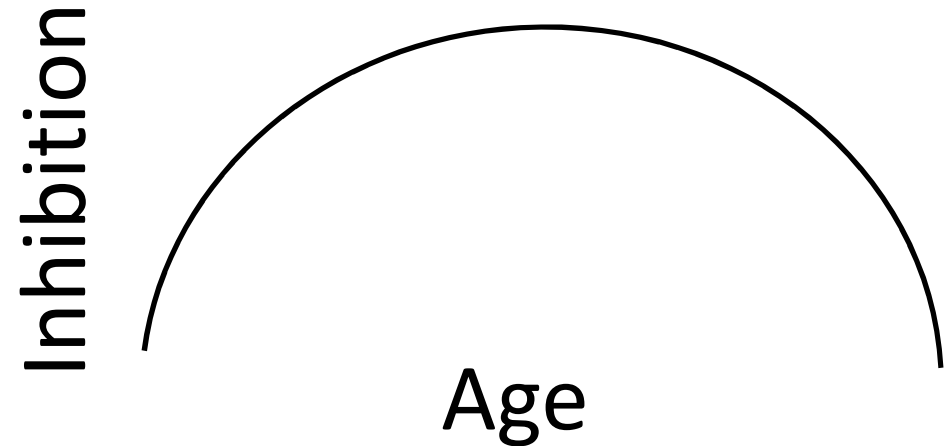
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- Inhibition & Development “Theory”
- Observations
- Relationship with Existing Theories
- Mechanistic Models for Psychological Phenomena

INHIBITION & DEVELOPMENT “THEORY”

3

- Strengthens in Childhood and weakens in Elderly
 - Curvilinear relationship with age
- Proposed by others
 - Lifespan: Dustman, ...
 - Childhood: Bjorklund & Harnishfeger, Garon, ...
 - Aging: Hasher & Zacks, ...
- Strengths
 - Integrates findings
 - Accommodates diverse theories
 - Mechanistic Models



OBSERVATIONS: PHYSIOLOGY

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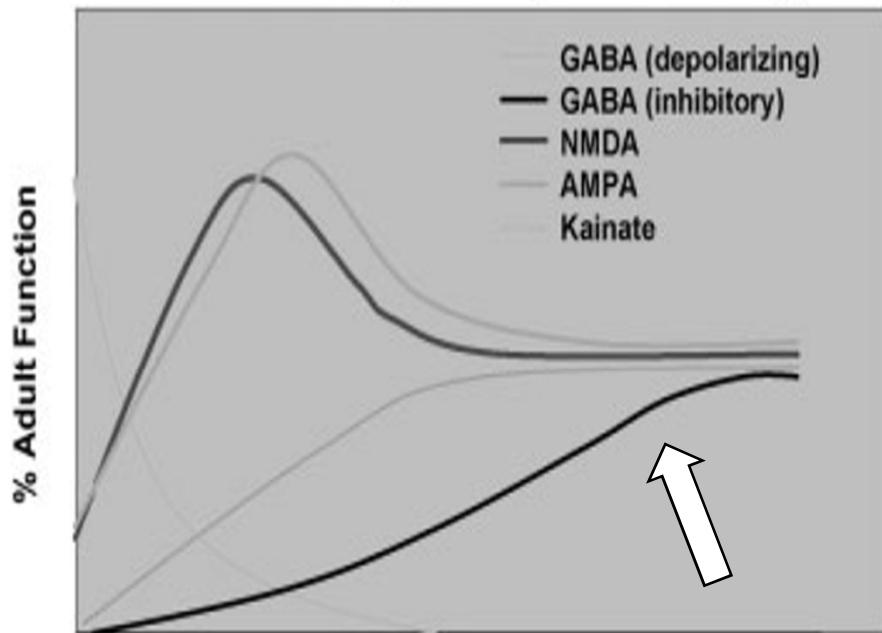
- Physiology
 - GABA
 - Seizures
 - Visual Evoked Potentials (VEPs)

GABA

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- Primary inhibitory neurotransmitter in mature brain
- GABA (Silverstein & Jensen, 2007): Inhibitory function strengthens over early years ←
- Postnatal Shift (Peerboom & Wierenga, 2021)
- Implicated in numerous cognitive and other psychological phenomena (Li et al, 2022)

Neuronal Receptor Expression vs Age



Rodent	P0	P5	P10	P15	P20	P25	P30	Adult
Human	20	30	40	1-2	>3			Adult
	PCW	PCW	PCW	years	years			

GABA

- Decline in GABA across lifespan (Gao et al, 2013)
→
- Steeper in later years?

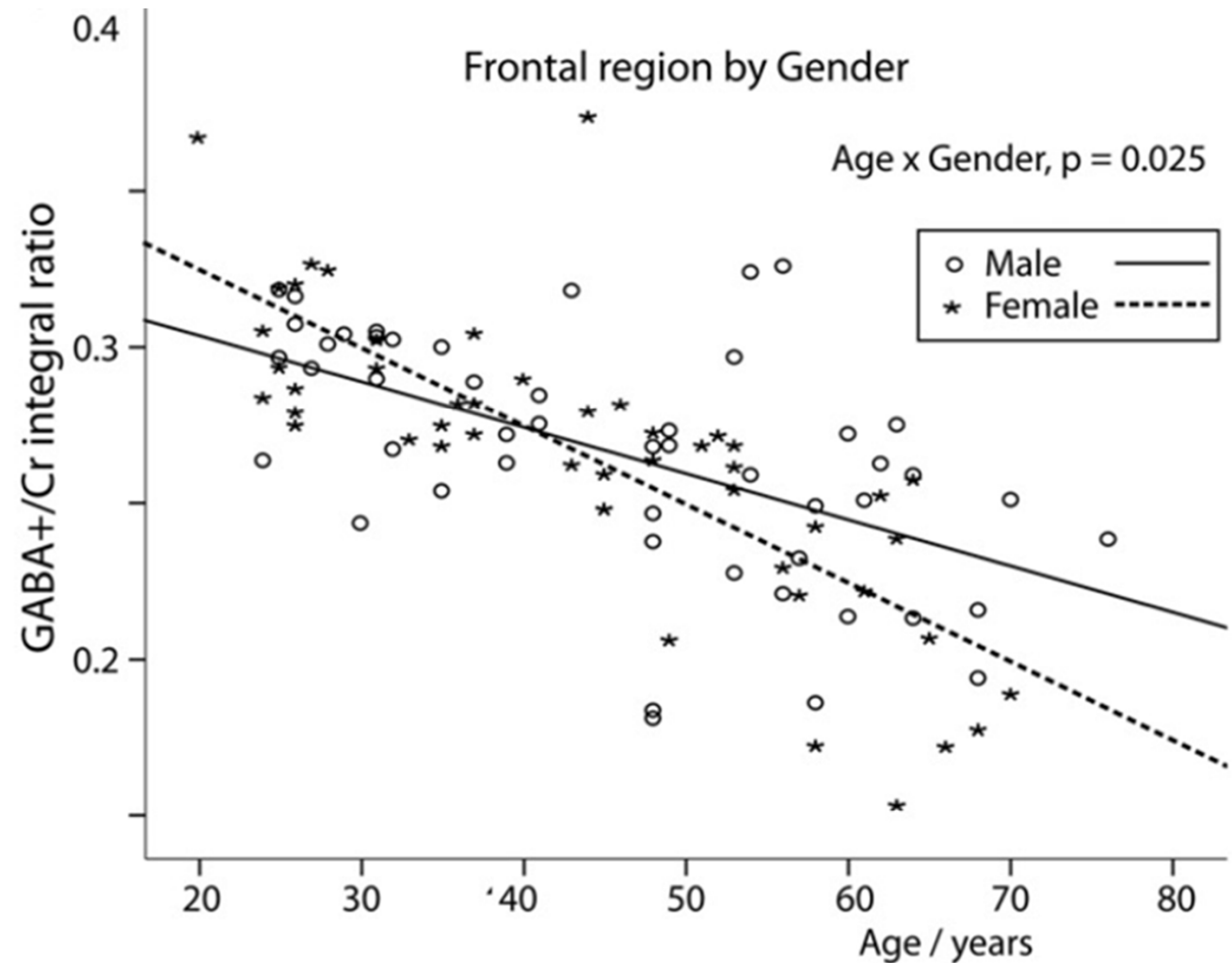


Fig. 3. Age-related decreases in GABA+/Cr ratio in the frontal region (a) and parietal region (b) from all the subjects. (c) Age-related decreases in GABA+/Cr ratio in the men and women in the frontal region (men: $r = -0.56$, $p < 0.001$; women: $r = -0.78$, $p < 0.001$). P value of interaction in gender-by-age is 0.025.

Seizures

- Seizures: excess of excitation and lack of inhibition
- Curvilinear relationship with age (Cloyd et al, 2006)

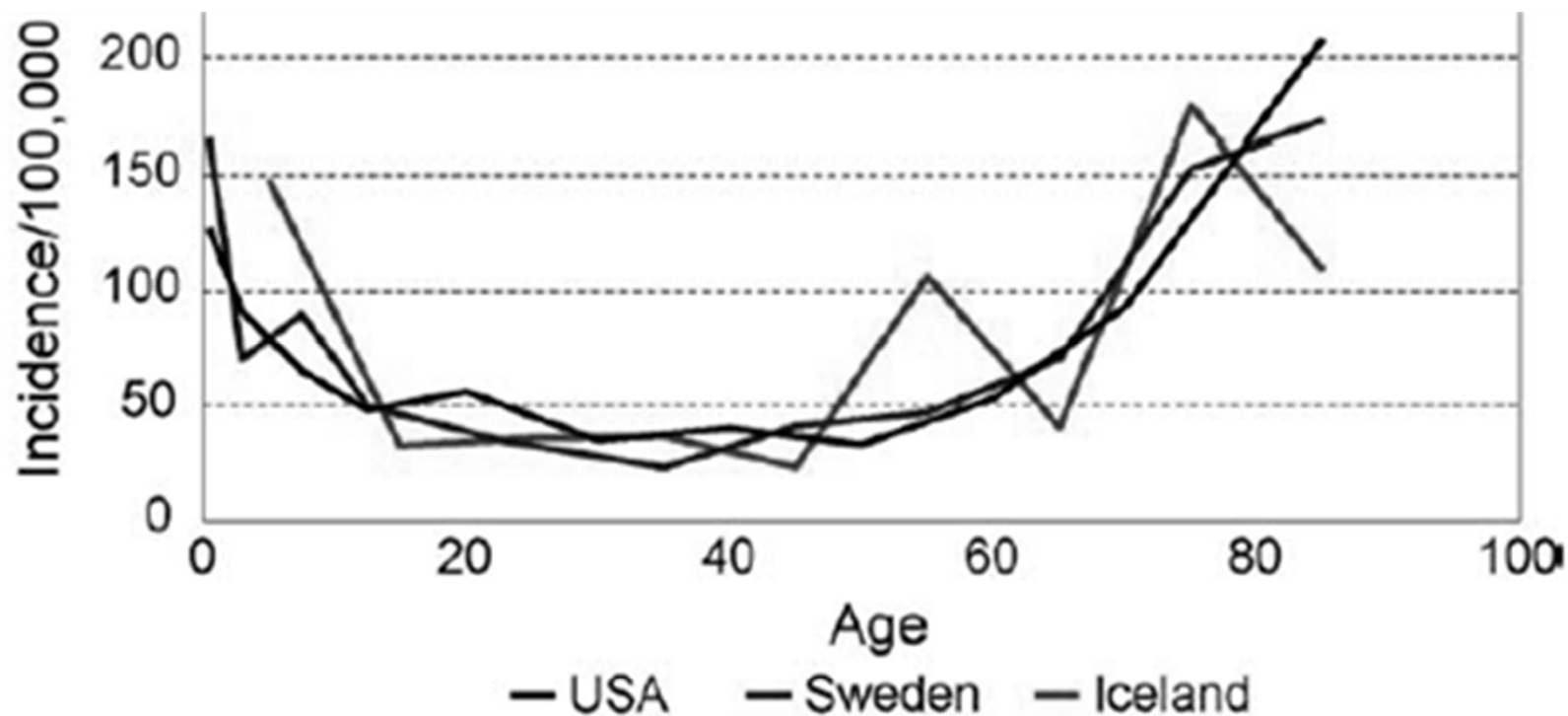
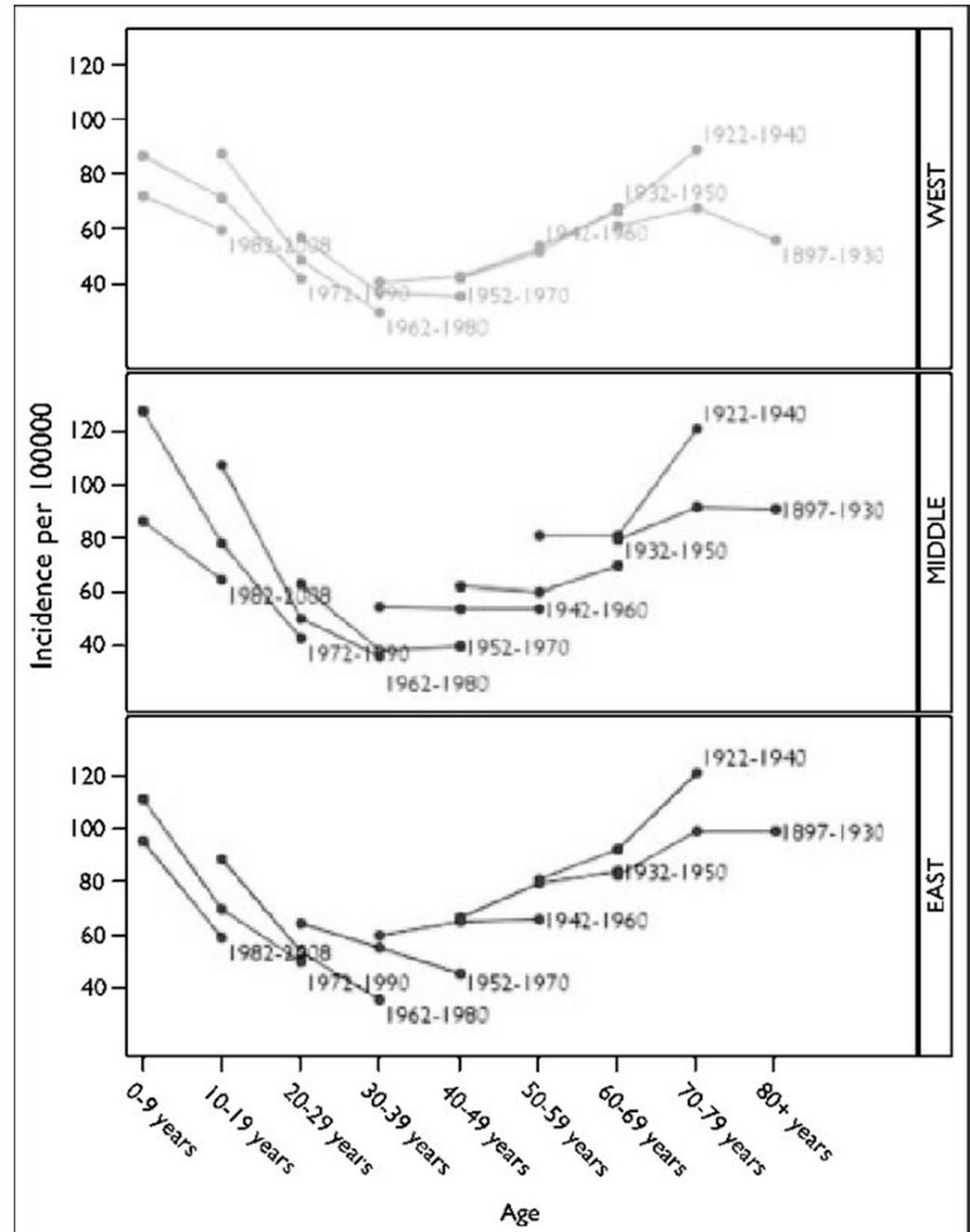


Fig. 1. Incidence of unprovoked seizures in developed countries (Hauser et al., 1993; Sidenvall et al., 1993; Forsgren et al., 1996; Olafsson et al., 2005).

Seizures

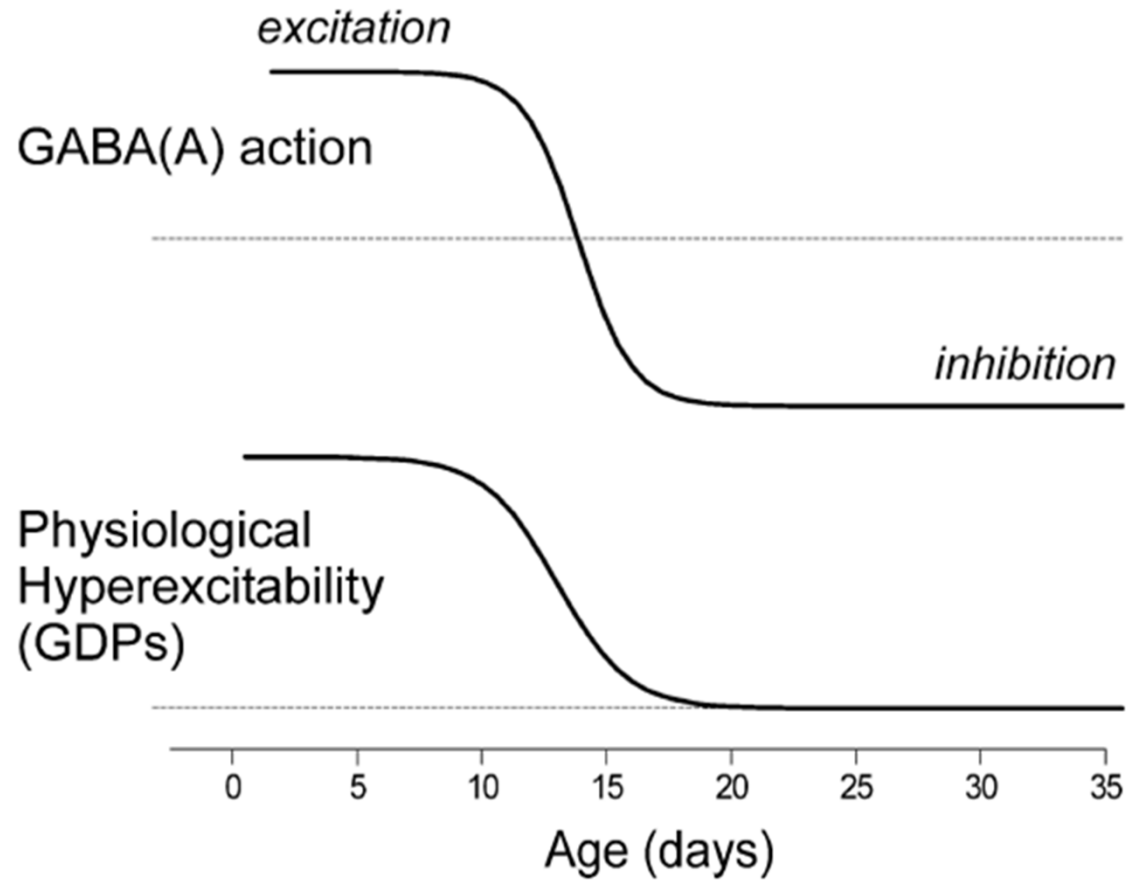
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- 23 Year study in three regions of Finland
- Track Anti-Epileptic Drugs in different cohorts and ages
- Decrease in childhood and increase in elderly: both by age and across time for cohorts (Sillanpää et al, 2011) →



GABA & Seizures

- Similar patterns with age in rats (Khazipov et al., 2004) →

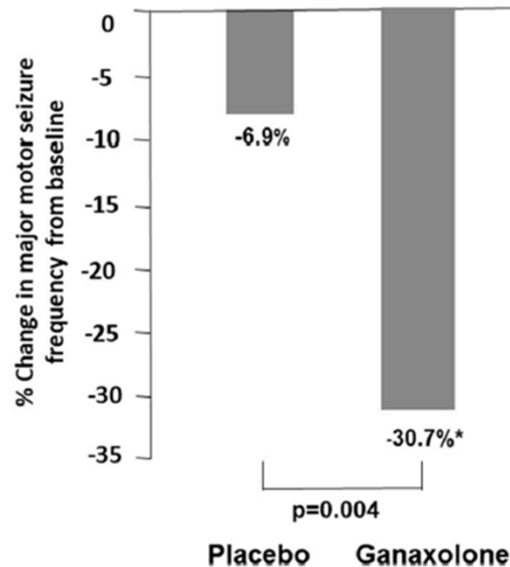


- Non-experimental

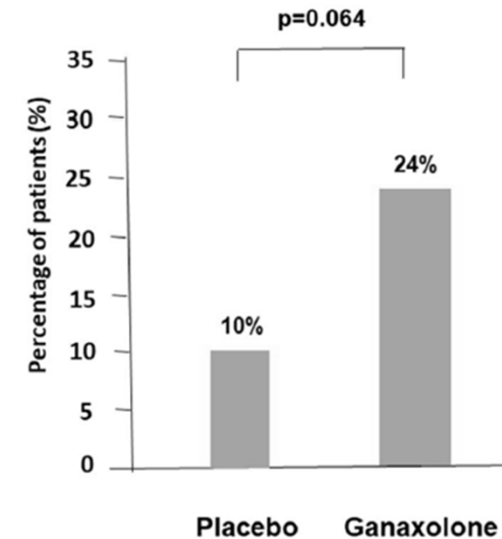
GABA & Seizures

- Medications that target GABA receptors (Perucca et al., 2023) →
- Experimental
- Dose-Response pattern

Median % change in major motor seizure frequency

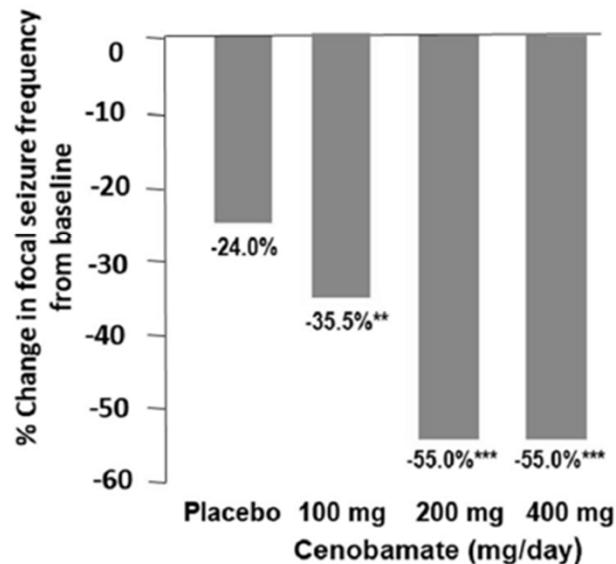


Responder rate

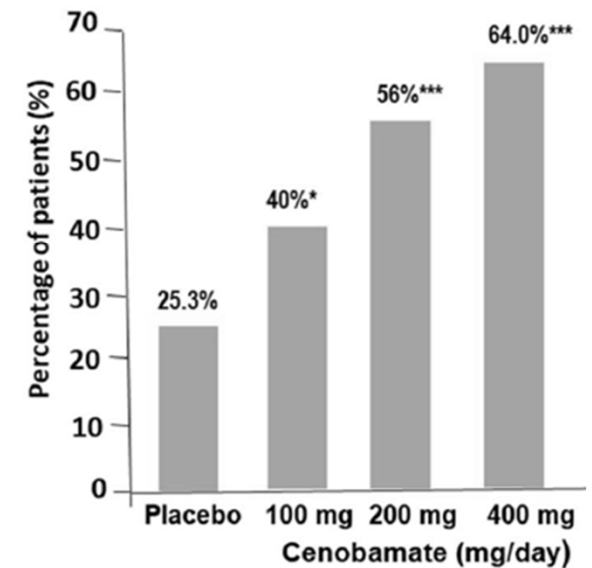


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Median % change in seizure frequency



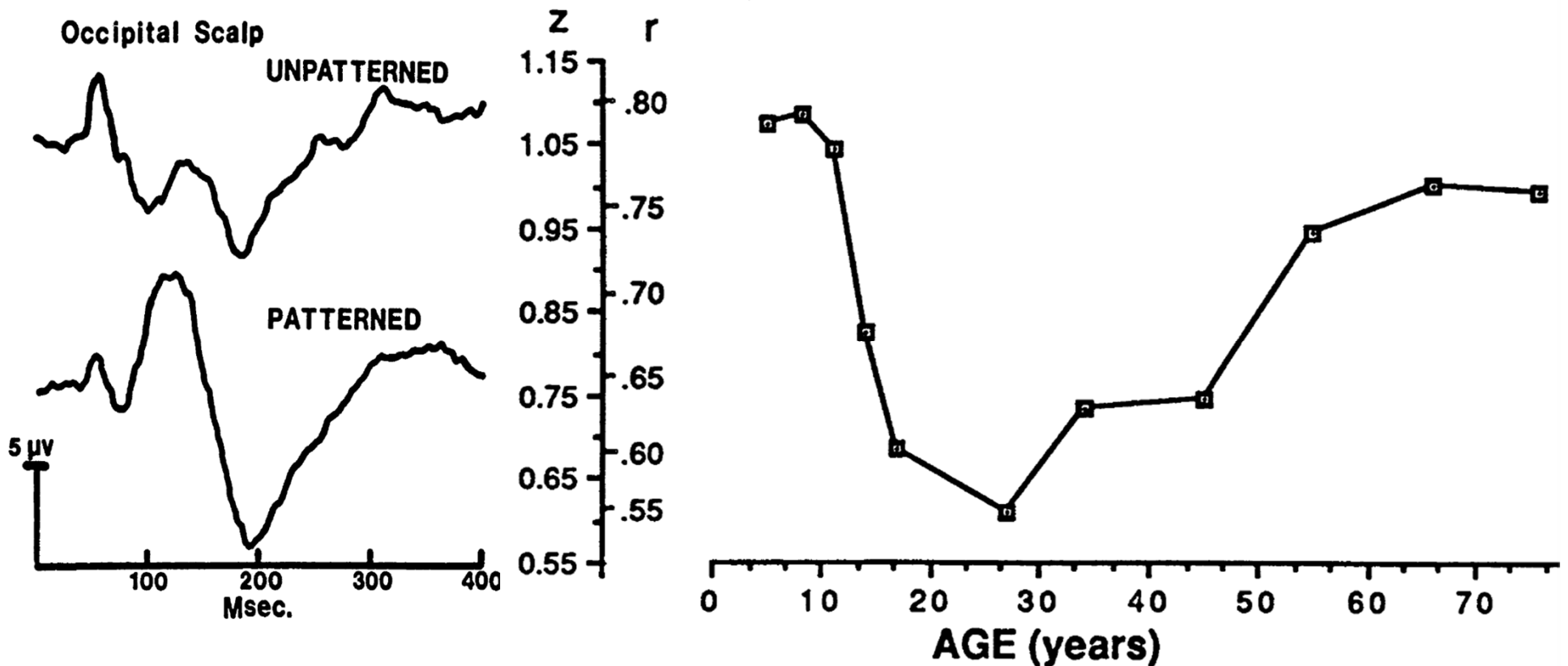
Responder rate (maintenance phase)



Visual Evoked Potentials

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- Visual Evoked Potential: Response of neurons to visual stimulation
- Patterned (checkerboard) versus Unpatterned stimulus
- Similarity reflects lack of inhibition (Dustman et al, 1996)



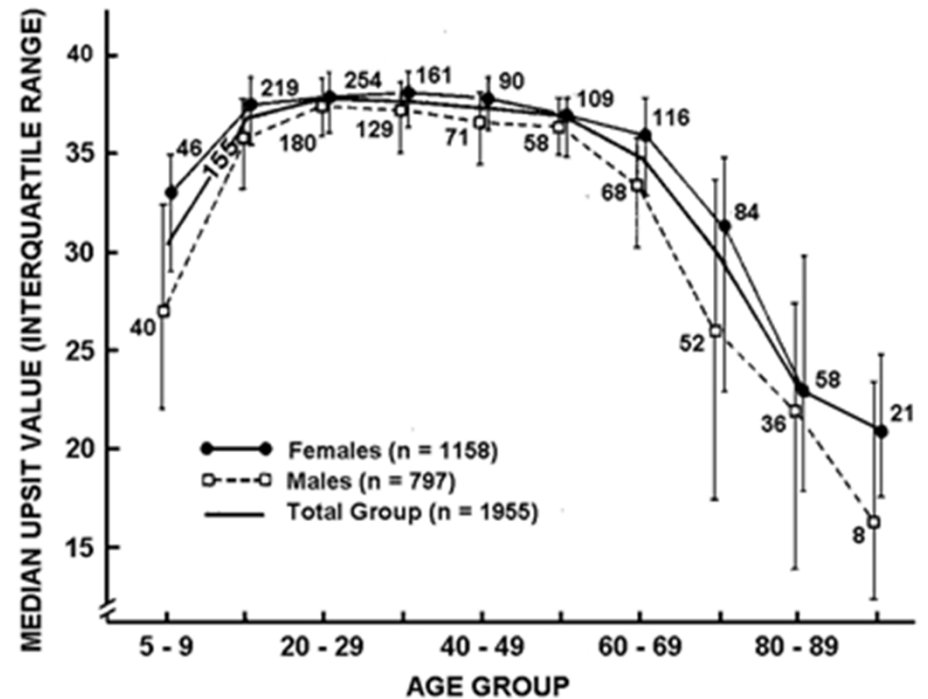
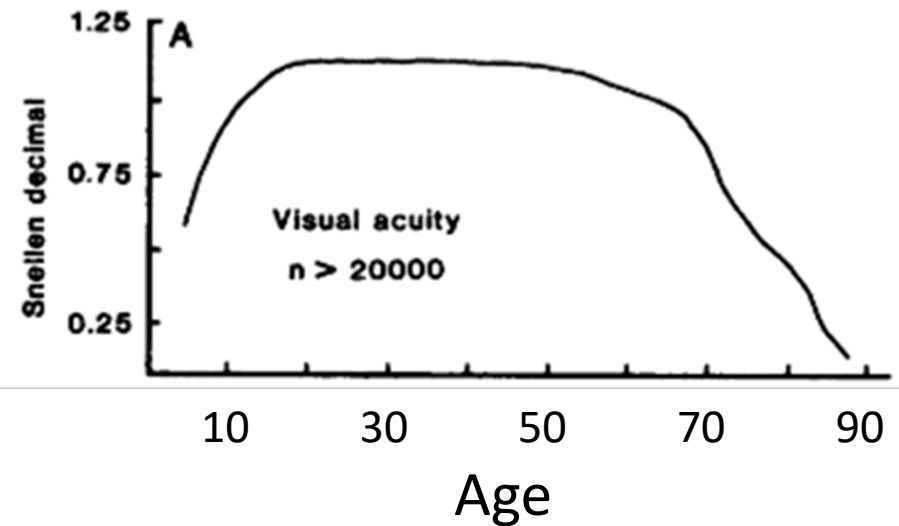
OBSERVATIONS: BEHAVIOURAL

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- Behavioural
 - Sensory Acuity
 - Anti-saccade task
 - Selective Attention
 - Interference
 - Impulsivity
 - Semantic Retrieval

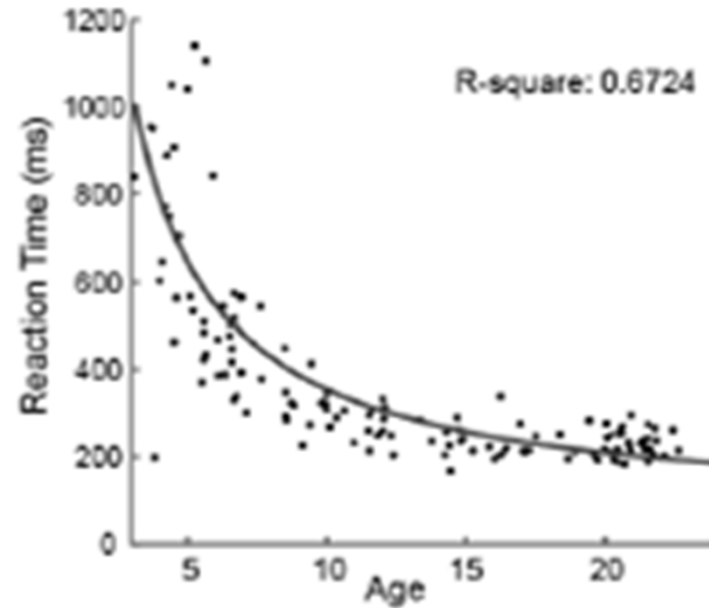
Sensory Acuity

- Curvilinear with age
- Visual (Pitts, 1982) (top)
- Smell (Doty et al, 1984) (bottom) & GABA (Attems et al, 2015)



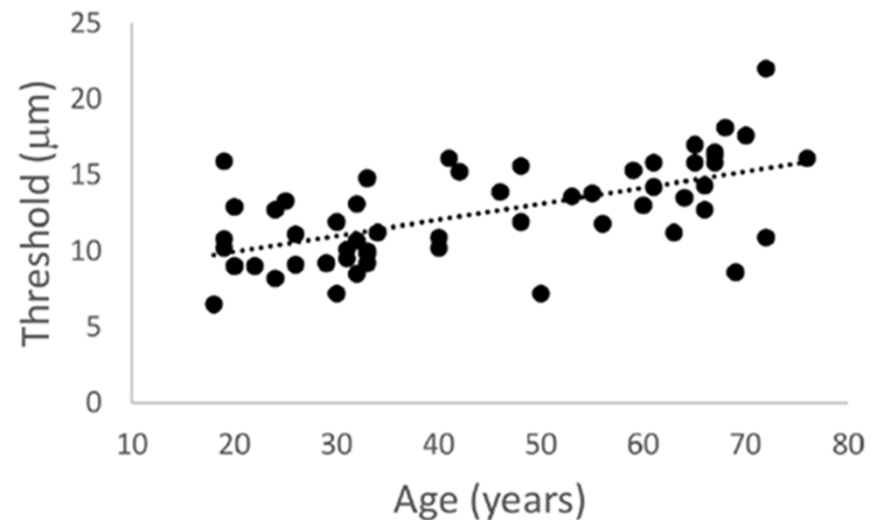
Sensory Acuity

- Tactile
- Childhood (Kaur et al, 2022) (top)
- Adulthood (Ruitenberget al, 2019) (bottom)



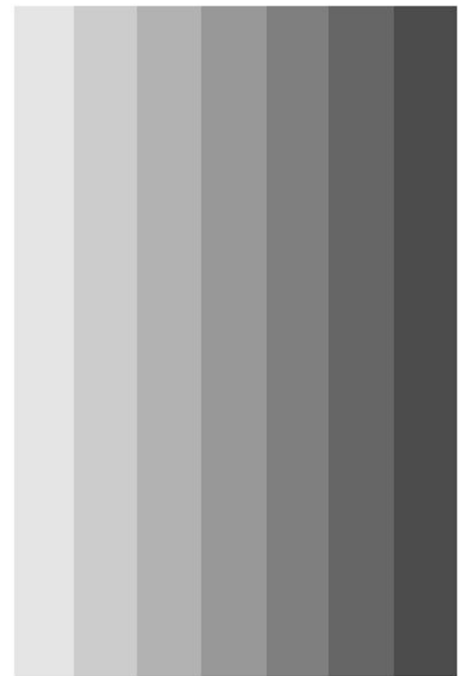
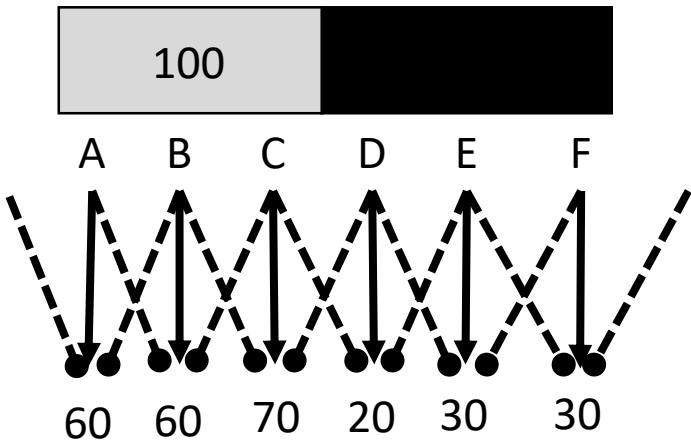
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Static threshold

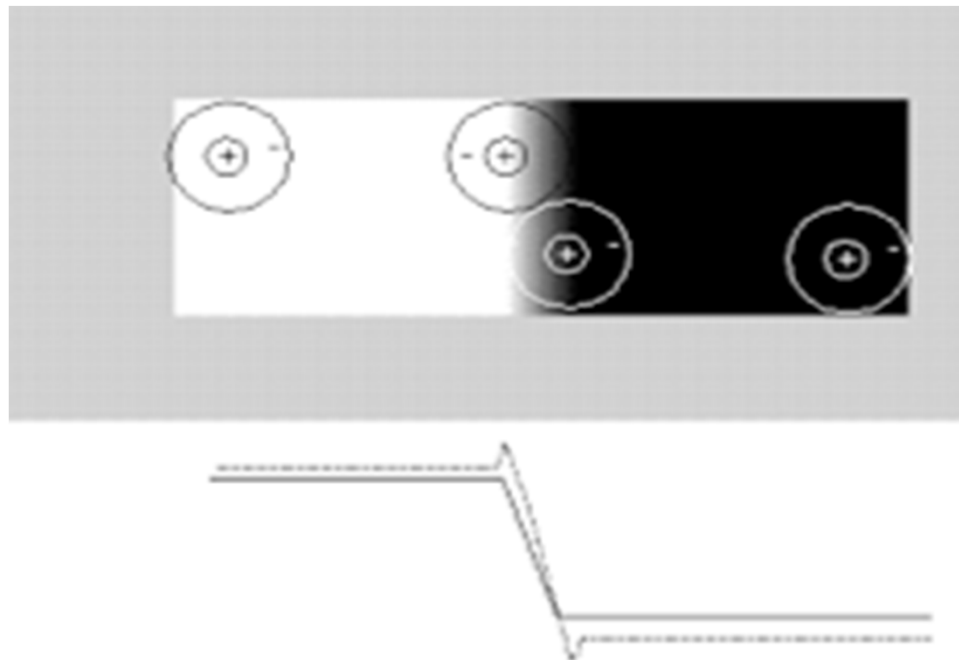


Inhibition & Visual Acuity

- Lateral inhibition enhances contrast at boundaries / edges
- VEPs



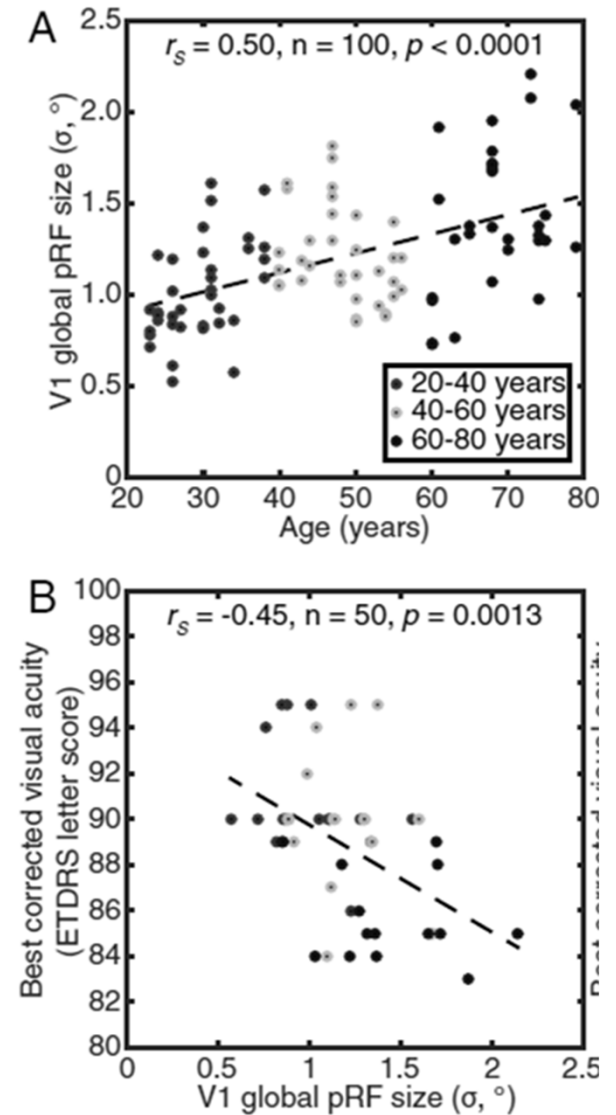
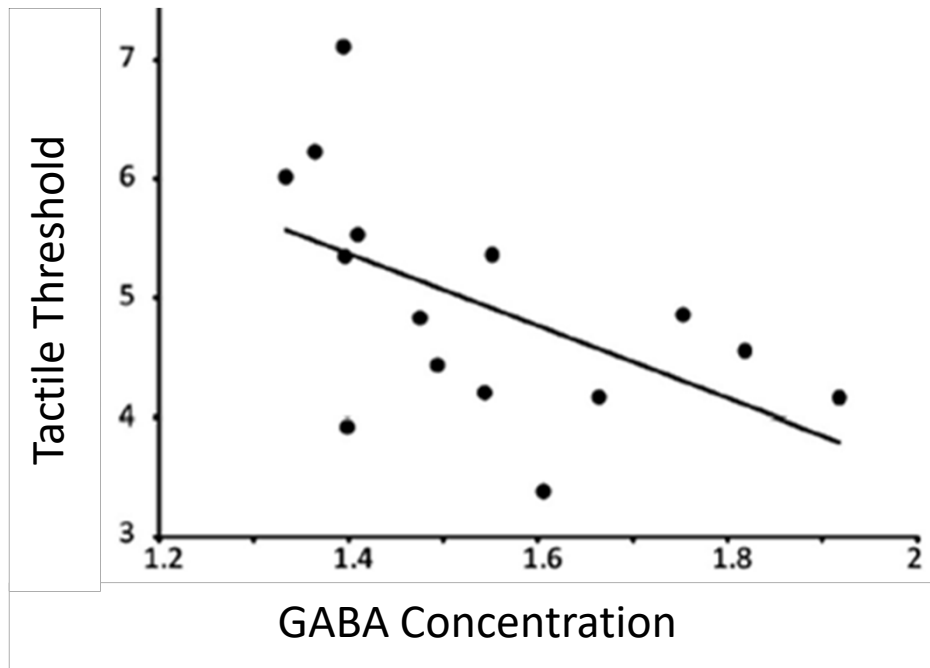
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Acuity & Inhibition

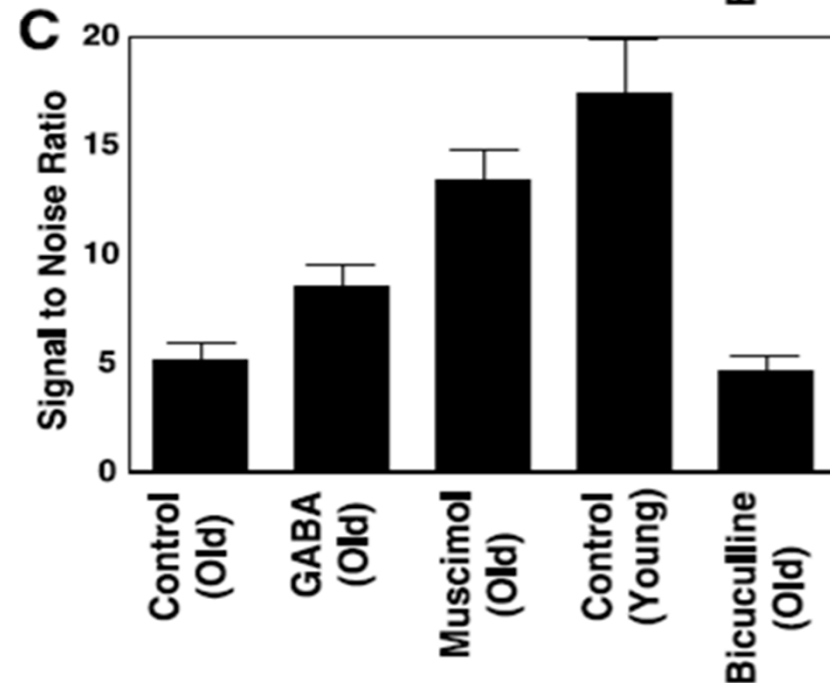
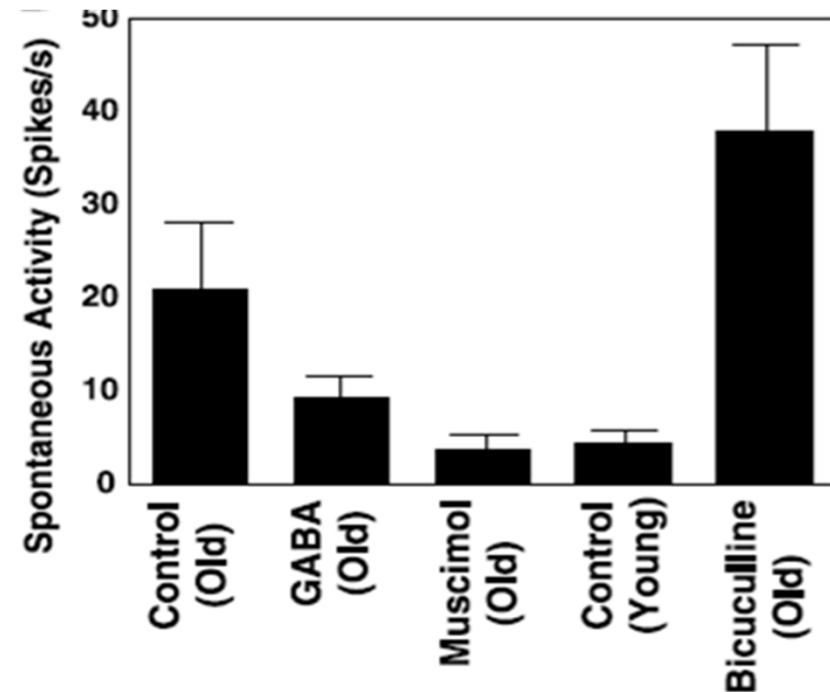
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- Visual acuity and receptive field size (Silva et al, 2021) (right): Wide receptive fields = weak lateral inhibition?
- GABA in Sensorimotor Cortex & Tactile Threshold (Puts et al, 2011) (below)



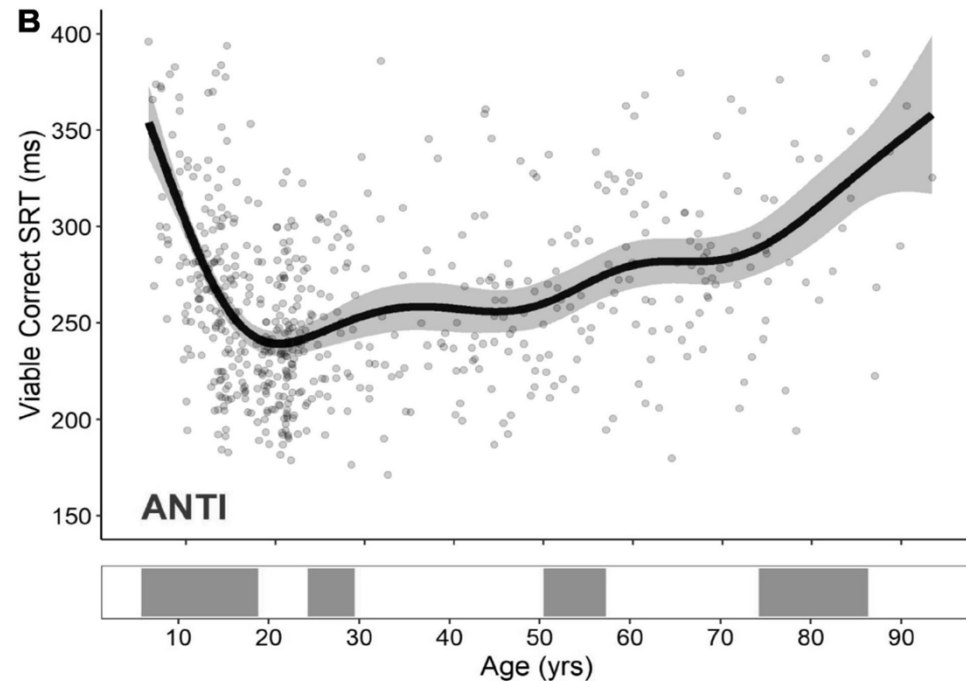
Acuity & Inhibition

- Old and young monkeys (Leventhal et al, 2003)
- Over-activation of visual cells in old (top) and low signal to noise ratio (bottom)
- Treatment for old
 - GABA or Muscimol (GABA agonist)
 - Bicuculline (GABA antagonist)

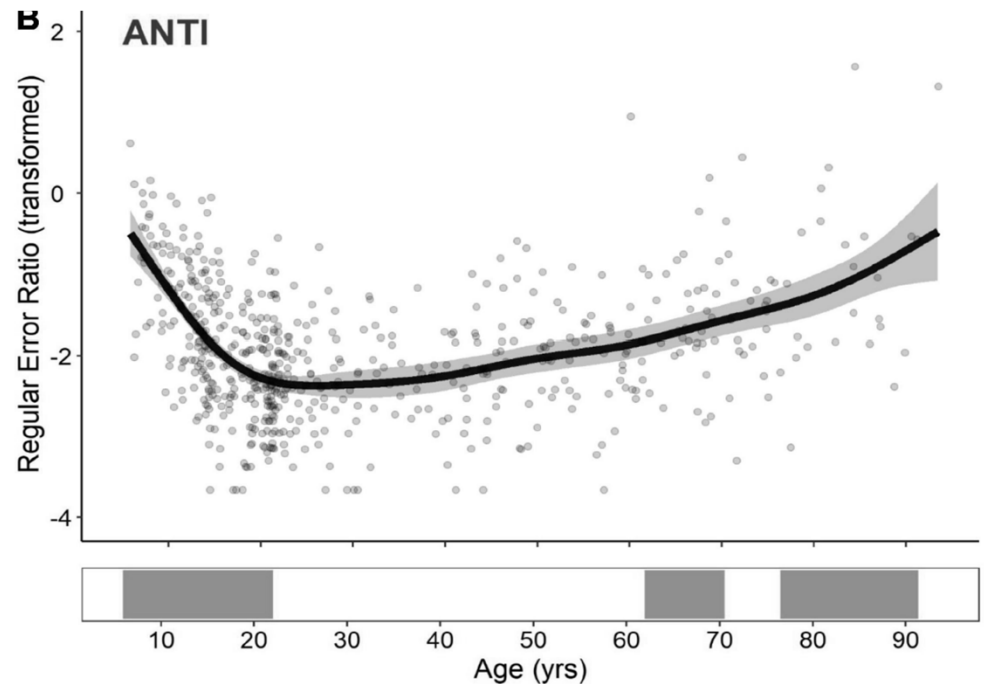


Anti-Saccade Task

- Stimulus shown on side of screen
- Position varies across trials
- Anti-Saccade: move eyes in opposite direction
- Slower (top) but still make more errors (bottom)
- (Yep et al, 2022)



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Selective Attention

- Stroop Task (Comalli et al, 1962)

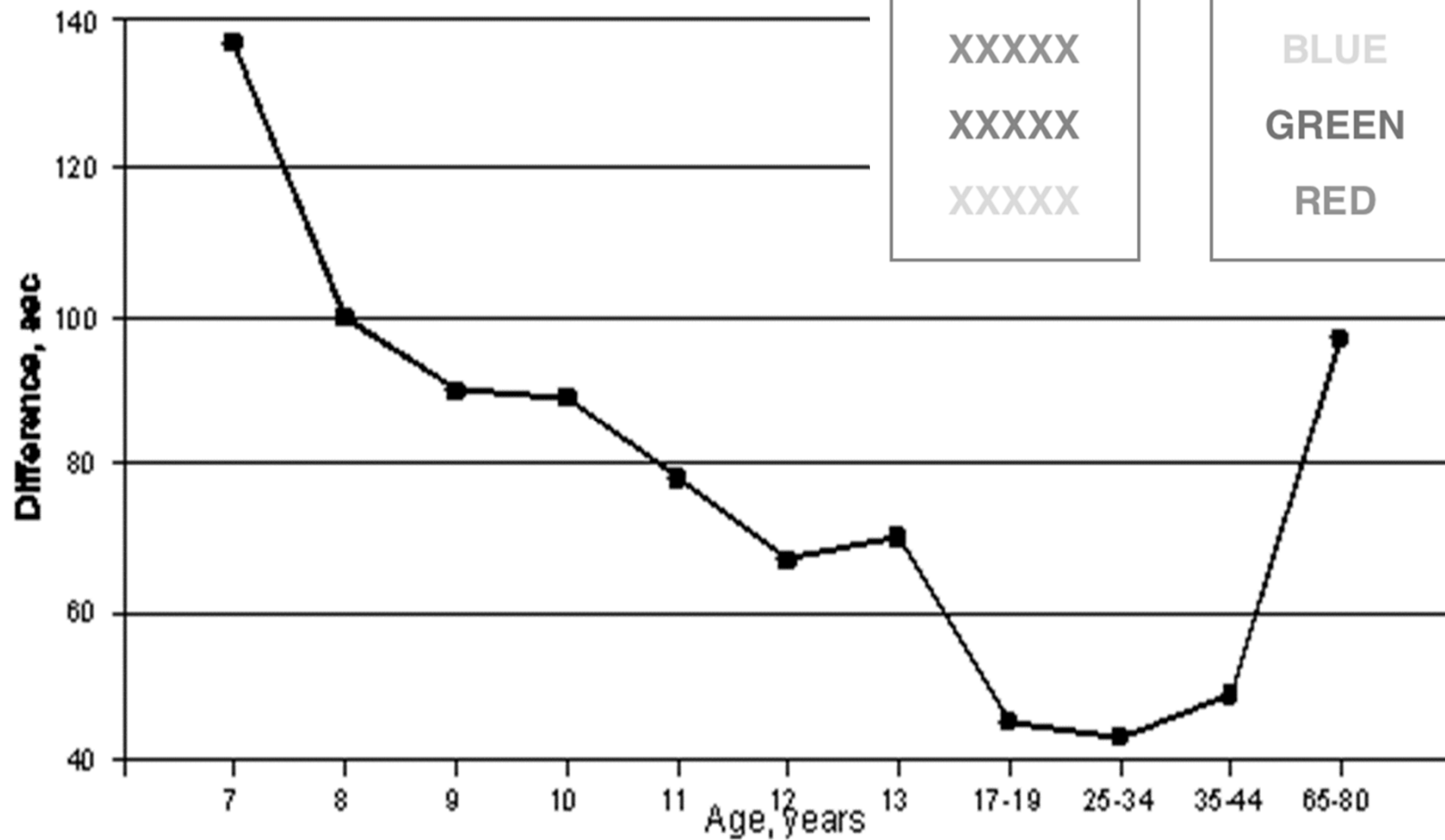
Control list:

XXXXX
XXXXX
XXXXX
XXXXX
XXXXX
XXXXX
XXXXX

Incongruent list:

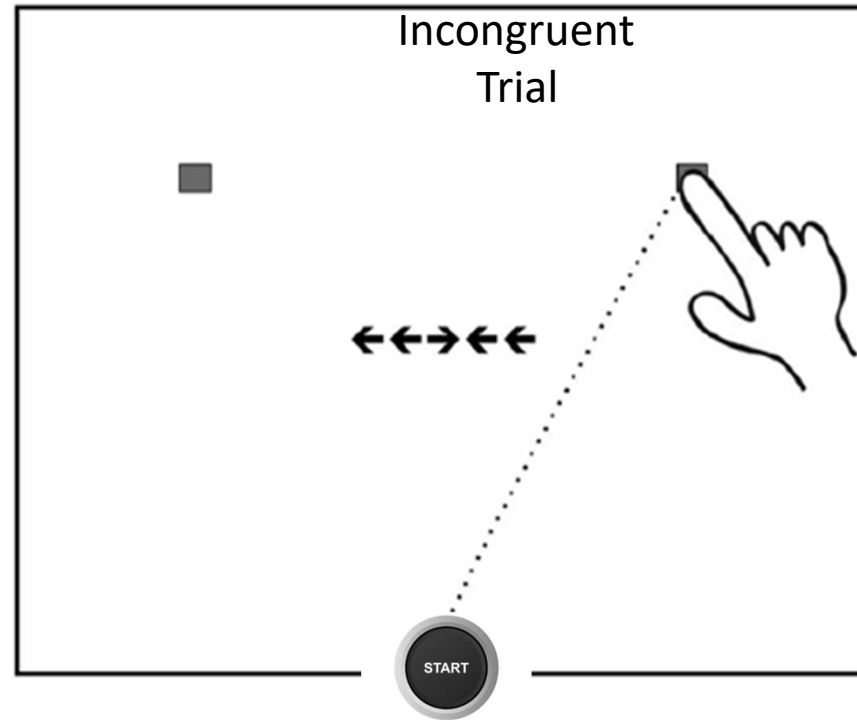
BLUE
YELLOW
GREEN
RED
BLUE
GREEN
RED

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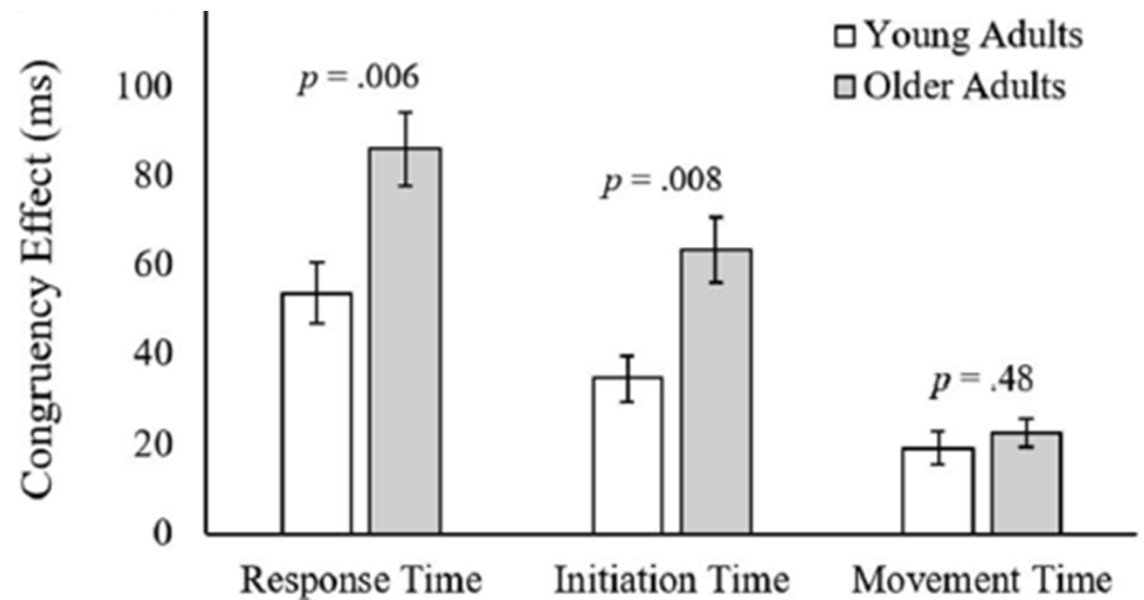


Interference

- Competing responses
- Flanker task (Erb et al, 2020)
- Congruent vs Incongruent stimuli on flanks
- Stronger effect for older adults
- Initiation time: time to release key to move

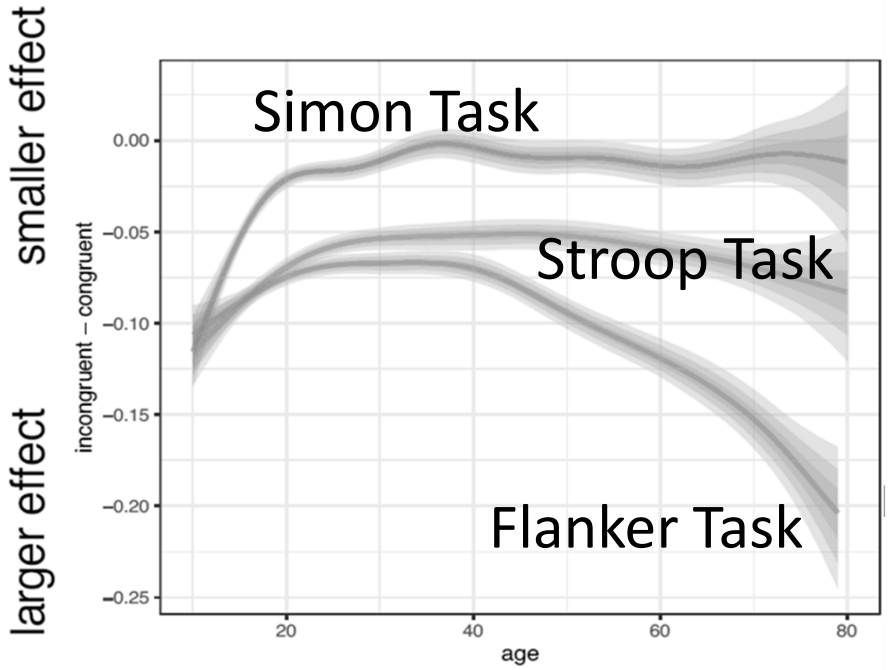
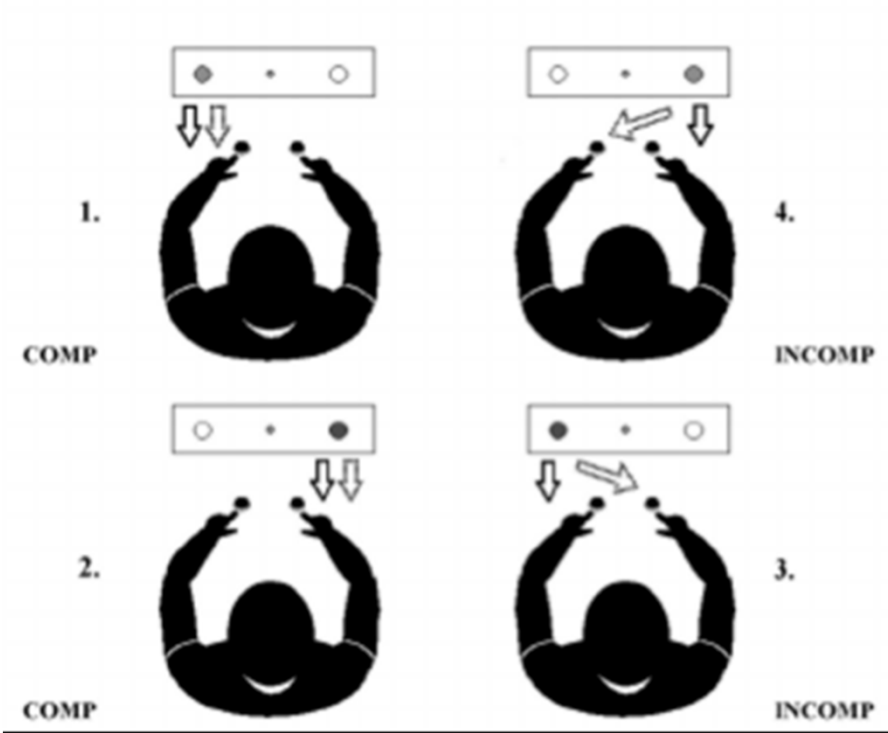


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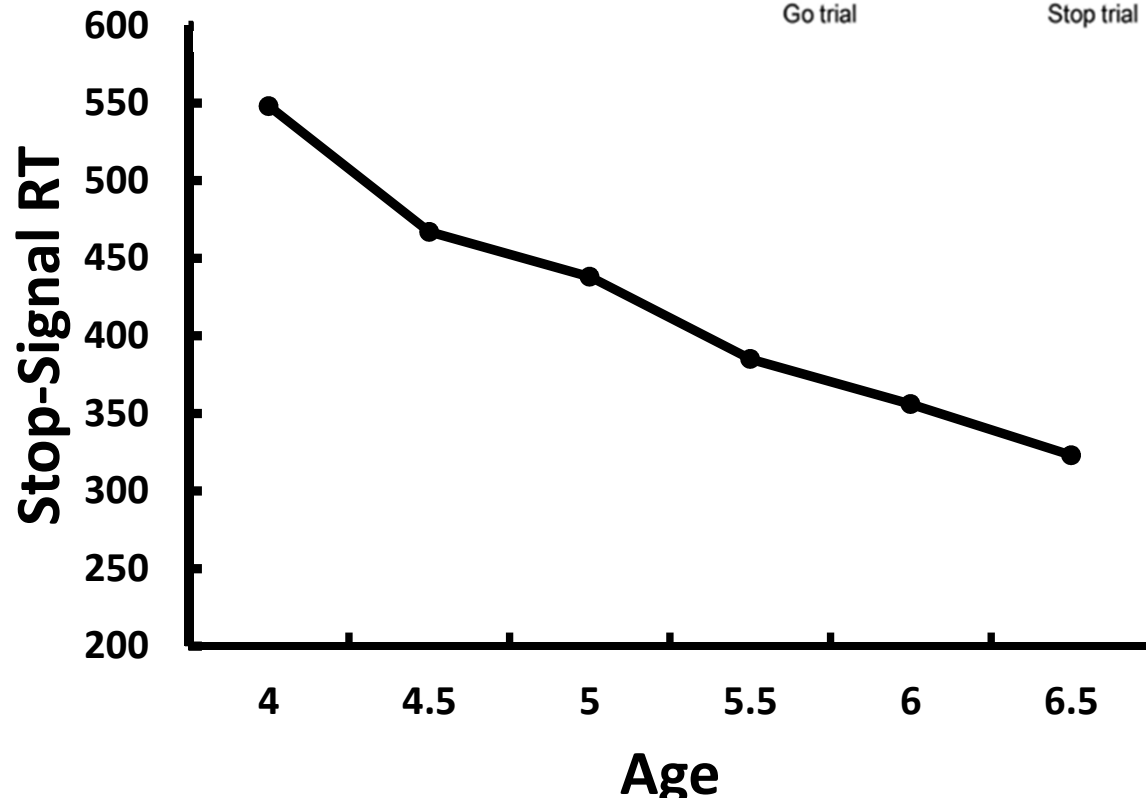
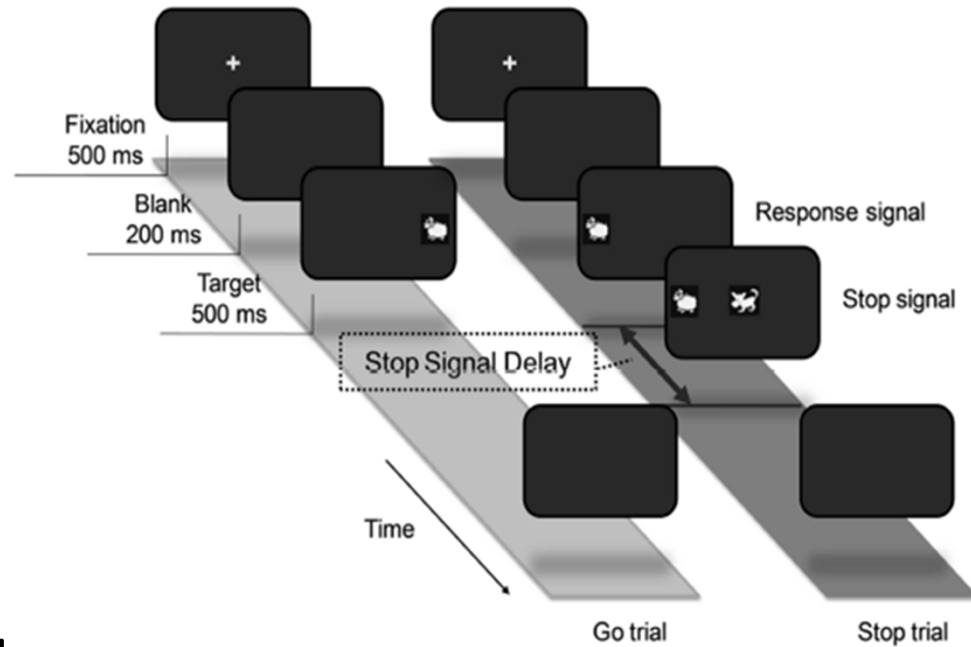
Interference

- Response competition
- Stroop, Flanker, Simon (top) (Erb et al., 2023)
- Also (Filippi et al, 2020; Gathercole et al, 2014)



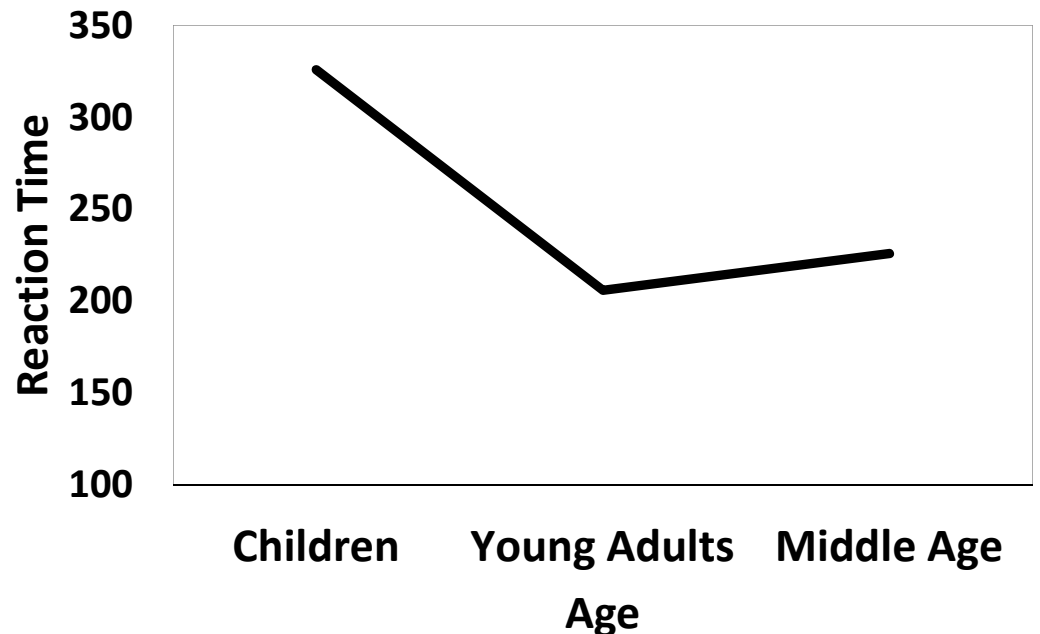
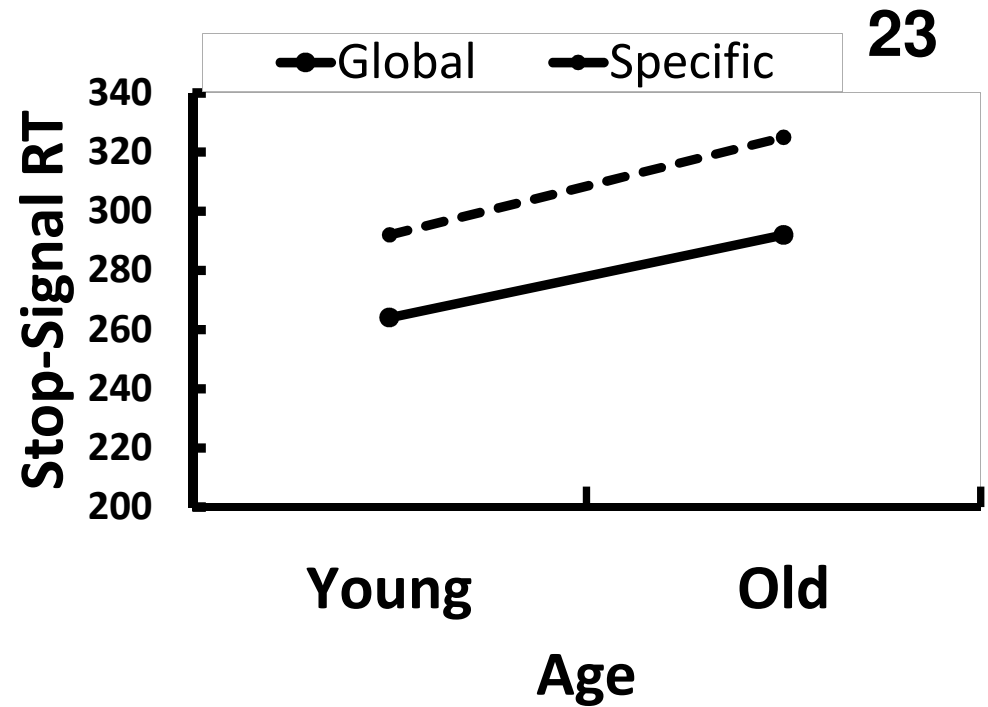
Impulsivity

- Tasks that involve inhibiting responses
- Stop-Signal RT Task (Lee et al, 2015)



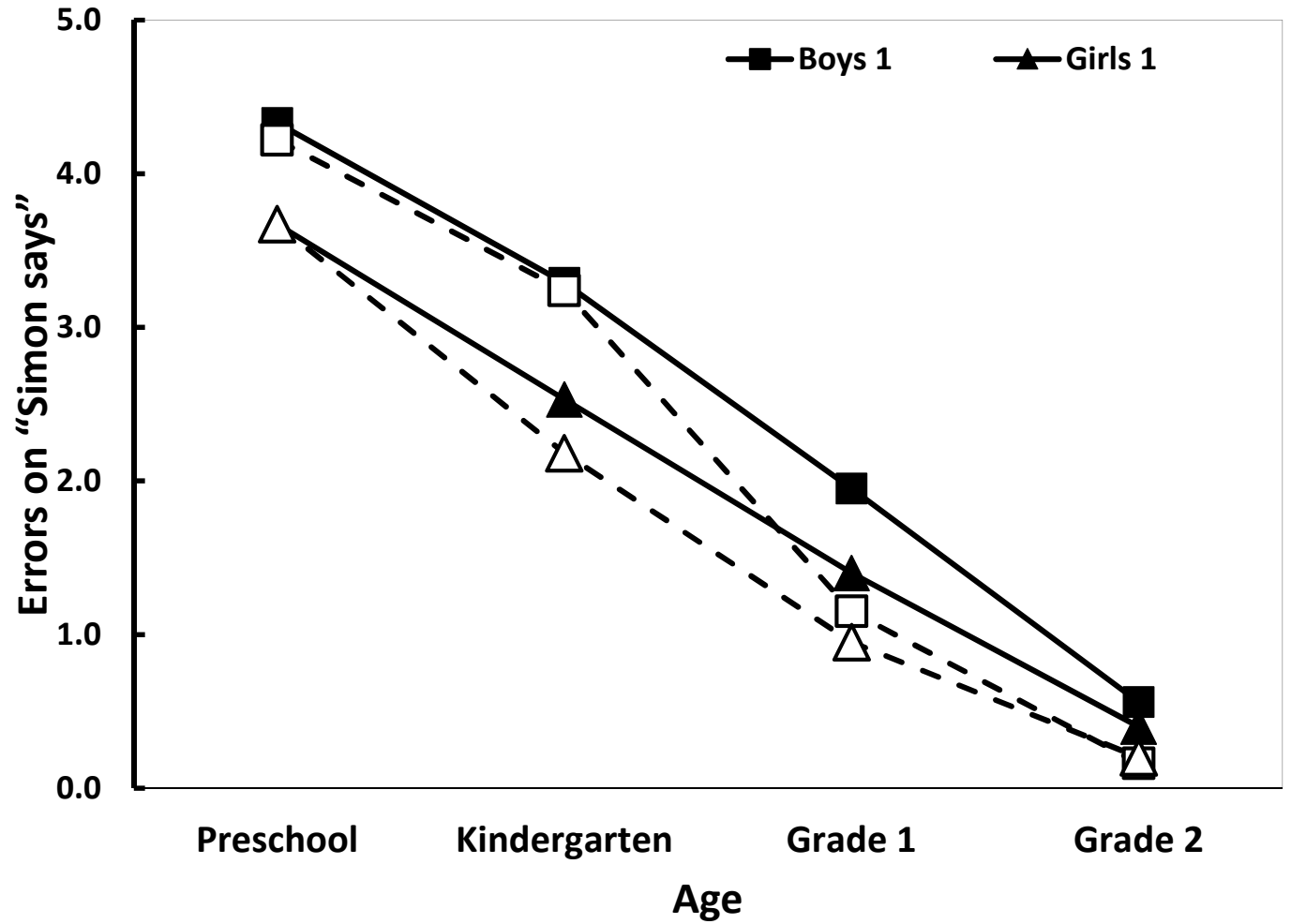
Impulsivity

- Stop-Signal RT in adults
- Hsieh & Lin (2019) (top)
- $r(\text{Age} \& \text{SSRT}) = .38$ (Sebastian et al, 2013)
- Dimoska et al (2007) (bottom)



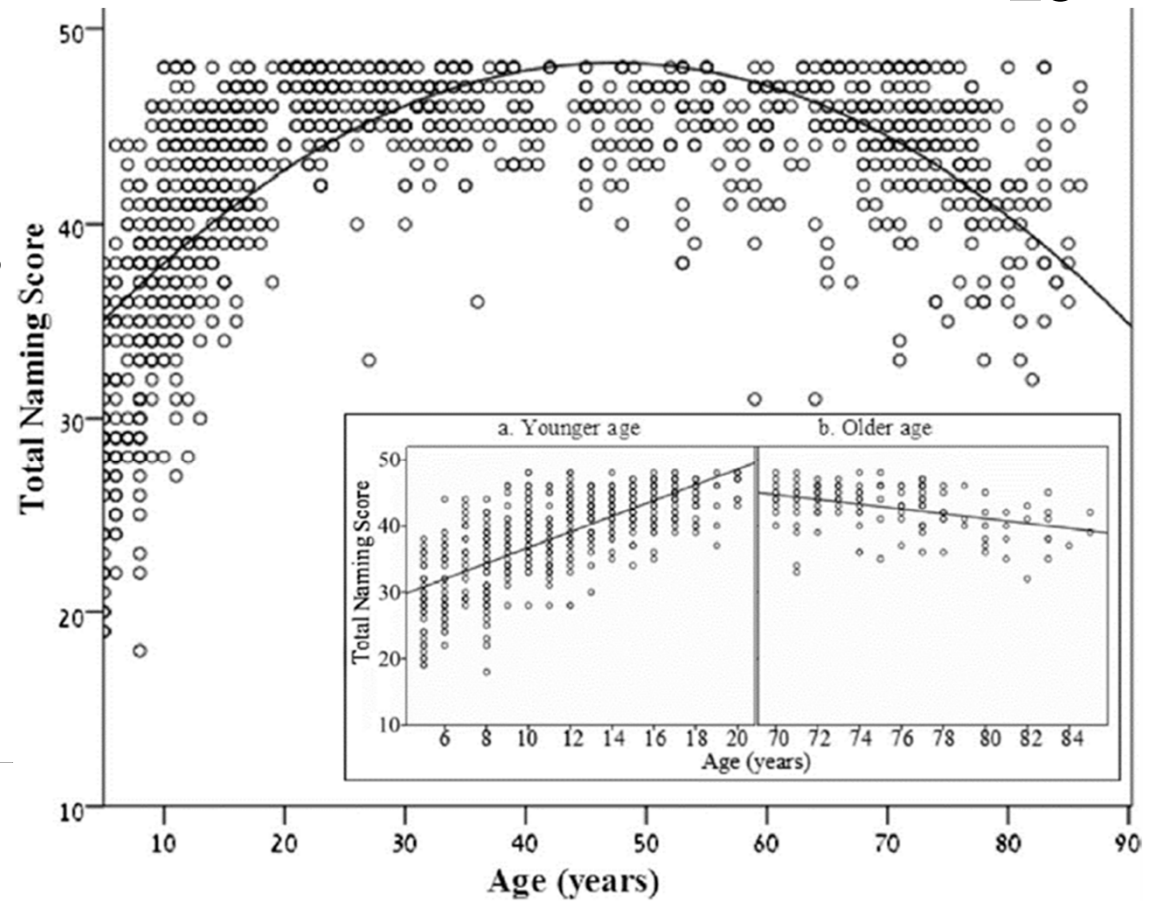
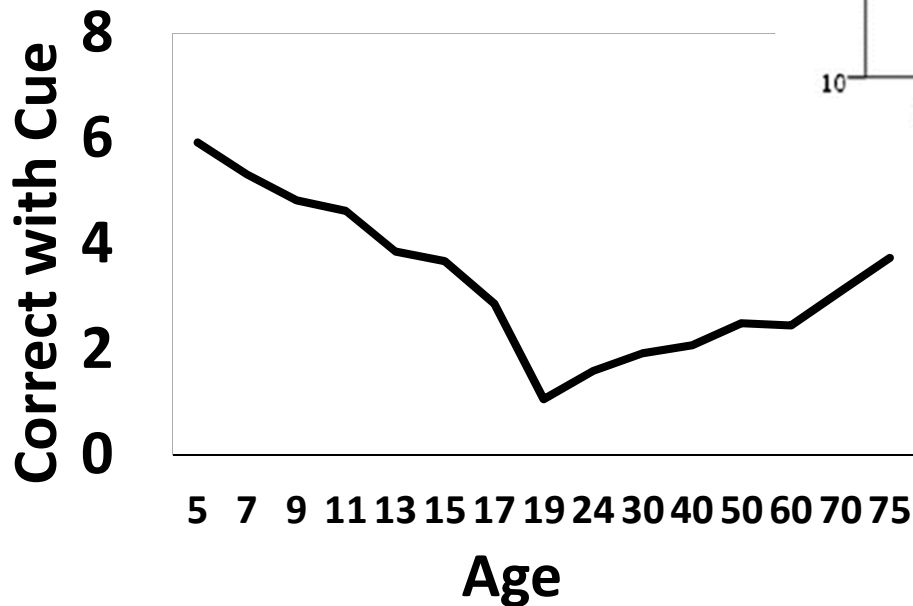
Impulsivity

- Simon Says (Strommen, 1973)



Semantic Retrieval

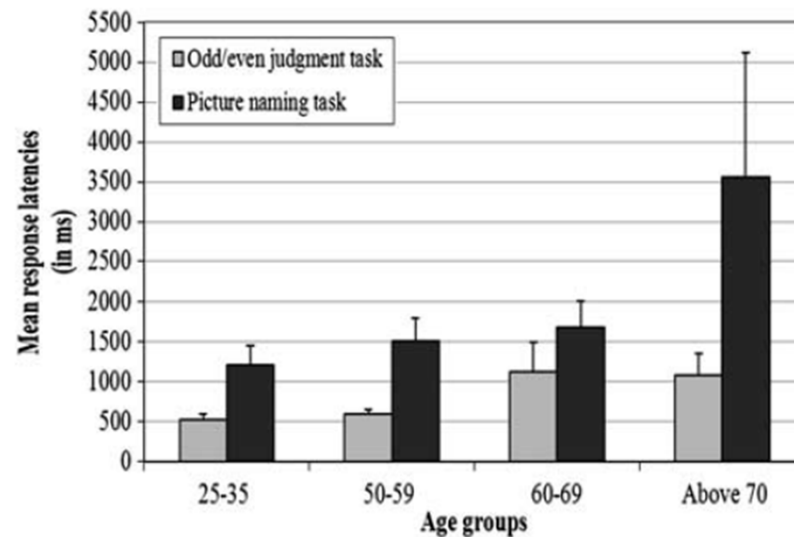
- Name 48 line drawings (Kave et al, 2010)
- Correct (top)
- Cued (bottom)



Semantic Retrieval

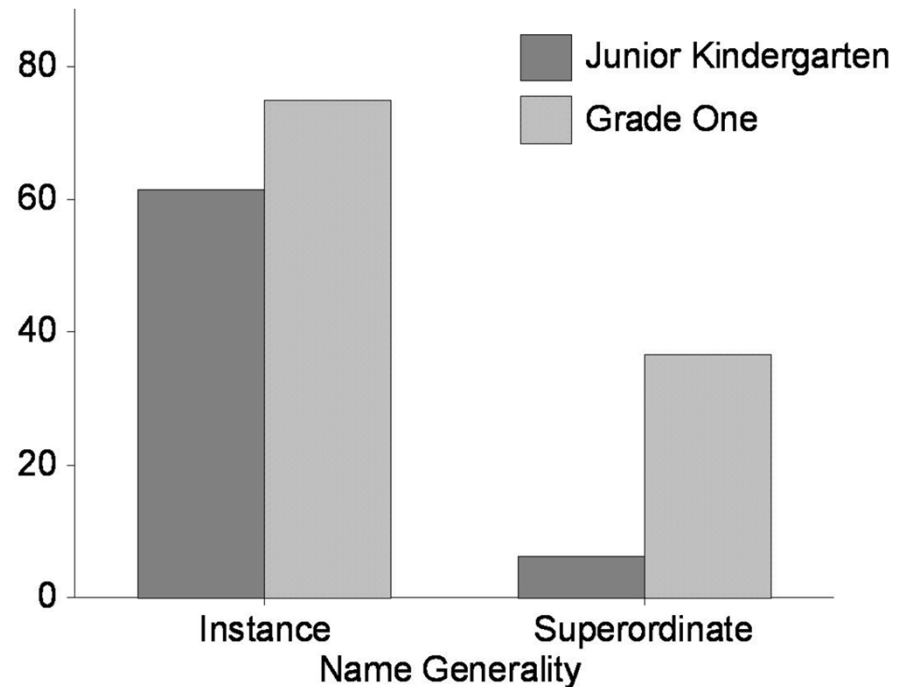
- Picture Naming
- Summary of 25 studies (Goulet et al 1994) (top)
- Verhaegen & Poncelet (2013) (bottom) also fewer correct responses

Authors	Age-related decline	Age groups (years)
Albert et al., 1988	yes	30-39; 50-59; 60-69; 70-80
Ardila & Rosselli, 1989	yes	55-60; 61-65; 66-70; 71-75; 76+
Au et al., 1990	yes	30-79
Bachy-Langedock, 1988	yes	20-34; 35-49; 50-64; >64
Béland & Lecours, 1990	no	19-49; 50-69; 70-87
Borod et al., 1980	yes	25-39; 40-49; 50-59; 60-69; 70-85
Bowles et al., 1987	yes	30-39; 70-79
Dordain et al., 1983	yes	<50; >50
Farmer, 1990	no	20-29; 30-39; 40-49; 50-59; 60-69
Flicker et al., 1987	no	18-30; 62-83
Goodglass, 1980a	yes	25-39; 40-49; 50-59; 60-69; 70-80
Kaplan et al., 1983	no	18; 20-29; 30-39; 40-49; 50-59
LaBarge et al., 1986	yes	60-64; 65-69; 70-74; 75-79; 80-85
Le Dorze & Durocher, 1992	yes	25-44; 45-64; 65-85
Metz-Lutz et al., 1991	yes	20-39; 40-59; 60-75
Mitchell, 1989	no	19-32; 63-80
Montgomery & Costa, 1983	yes	65-89
Nicholas et al., 1985	yes	30-39; 50-59; 60-69; 70-79
Nicholas et al., 1989	no	40-78
Poon & Fozard, 1978	yes/no	18-22; 45-54; 60-70
Rosselli et al., 1990	yes	16-25; 26-35; 36-45; 46-55; 56-65
Thomas et al., 1977	yes	25-35; 36-45; 46-55; 56-65; >65
Thuillard & Assal, 1989	yes	20-29; 30-39; 40-49; 50-59; 60-69; 70-79; 80+
Van Gorp et al., 1986	yes	59-65; 65-69; 70-74; 75-79; 80+
Villardita et al., 1985	no	15-24; 45-54; 55-64; 65-74

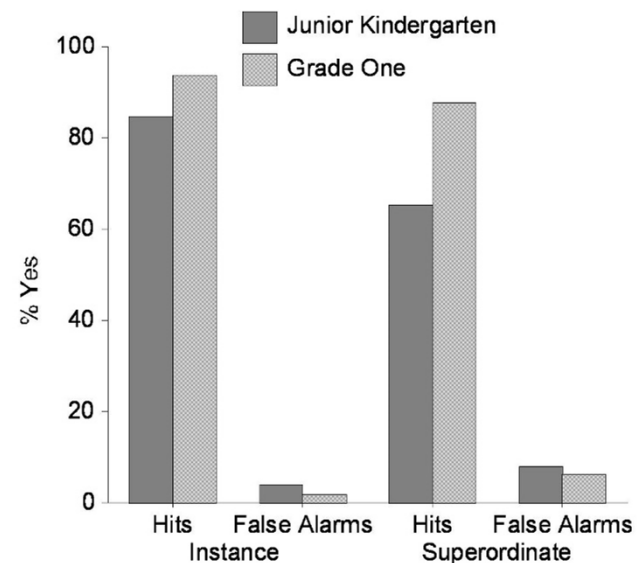


Semantic Retrieval

- Picture Naming Task
- Generate Instance Name (e.g., dog) or Category Name (e.g., animal)
- JK particular difficulty with retrieving category name (Clark & Johnson, 1994, top)
- Recognition task shows they “know” correct response (bottom)

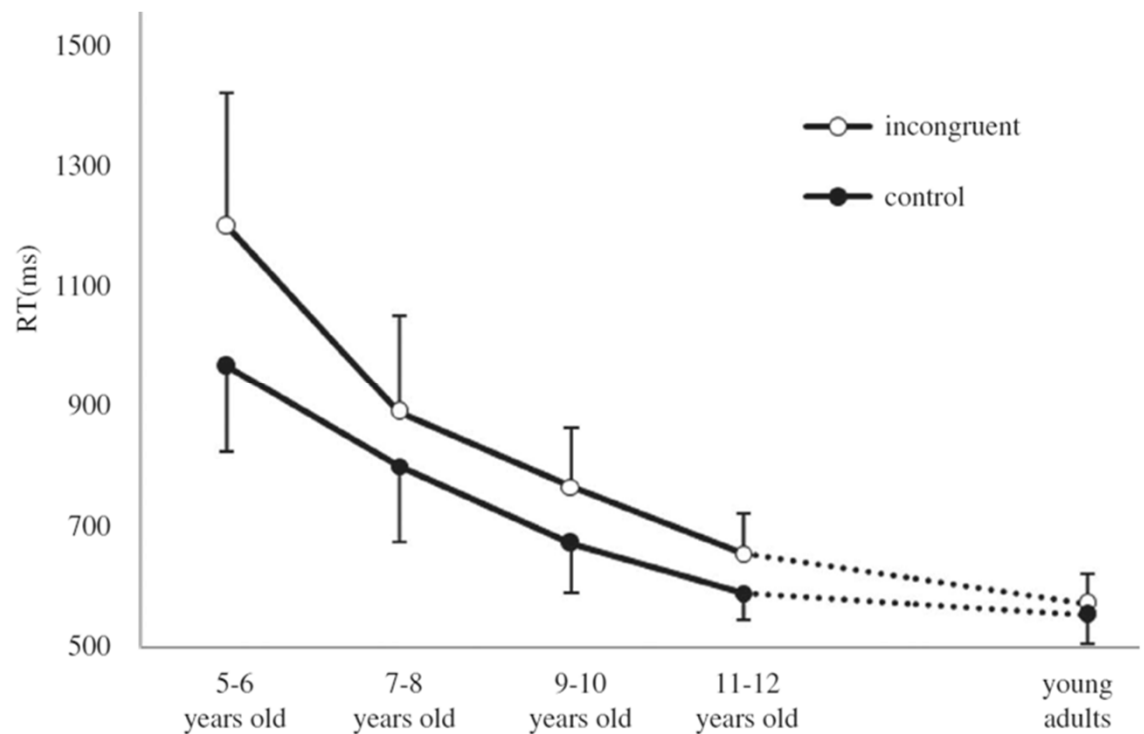
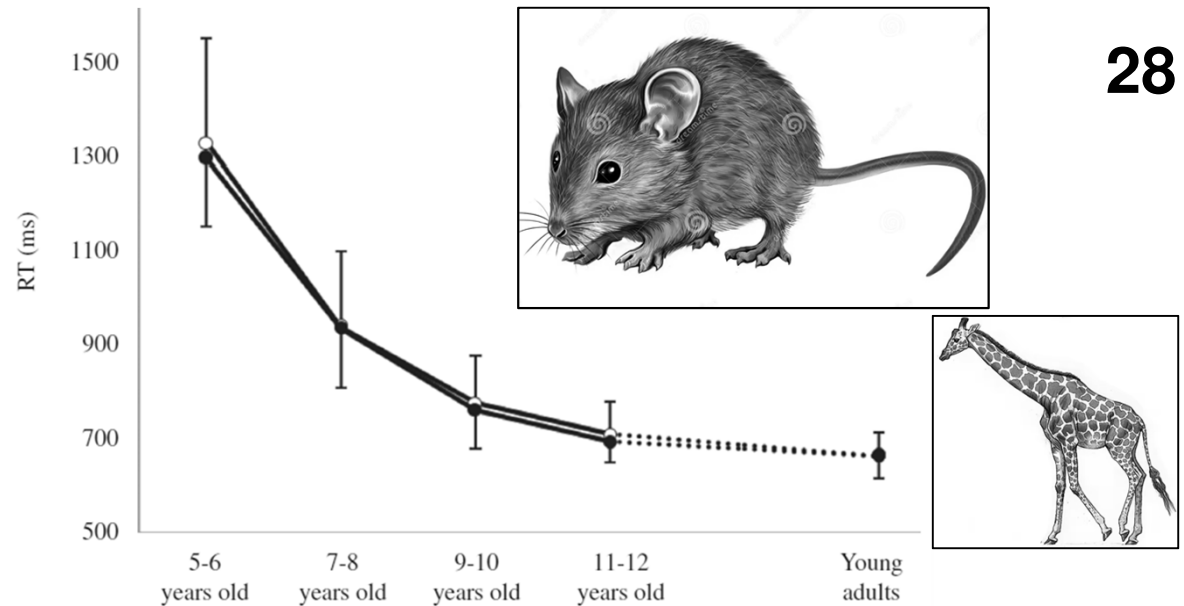


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Semantic Retrieval

- Ikeda et al, 2013
- Congruous or incongruous sized pictures of animals of different sizes
- Judge actual size: no interference (top)
- Judge picture size: need to suppress prepotent response (bottom)



Semantic Retrieval

- Shafto et al (2007) TOT $r = .43$ with age, negative r with grey matter
- GABA & Grey Matter (Jensen et al., 2005)



Singer and actress who is best known for her role as Dorothy in "The Wizard of Oz".

Figure 1. Example of a picture and caption used on a single trial in the TOT task.

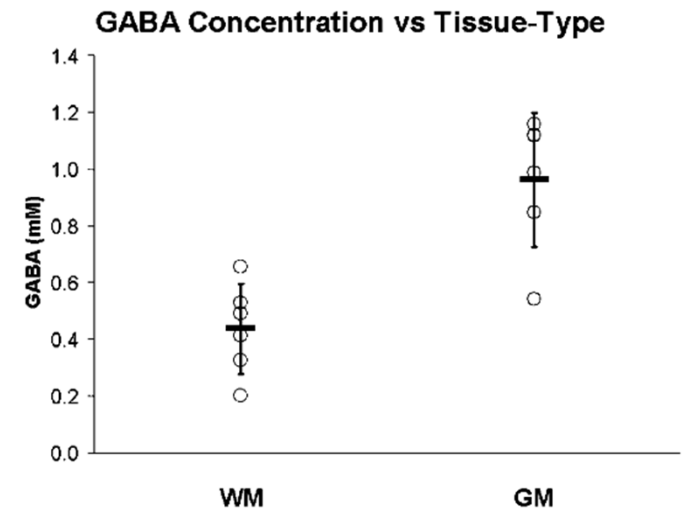
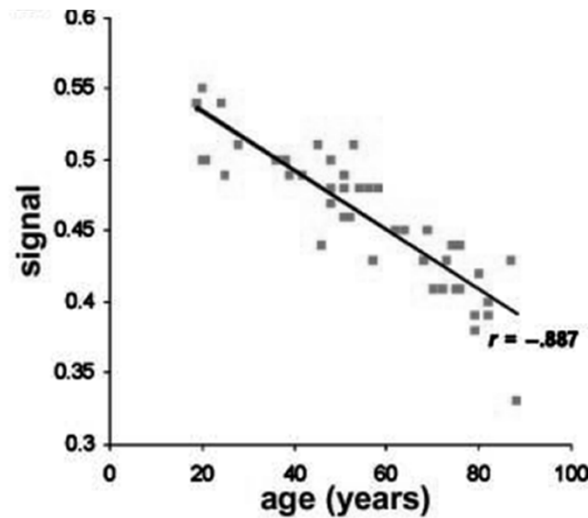
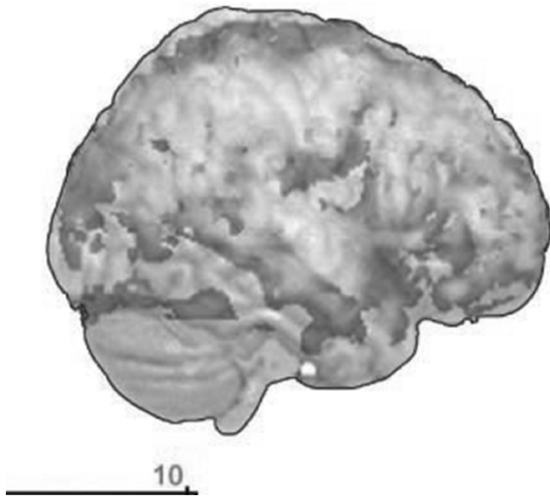


Figure 7. Scatterplot of brain GABA levels in cortical grey versus white matter in six healthy adult volunteers. Circles represent GABA level in each individual subject ($n = 6$), solid bars indicate group mean GABA levels and error bars represent group standard deviations of the mean

INHIBITION & ALTERNATIVE THEORIES

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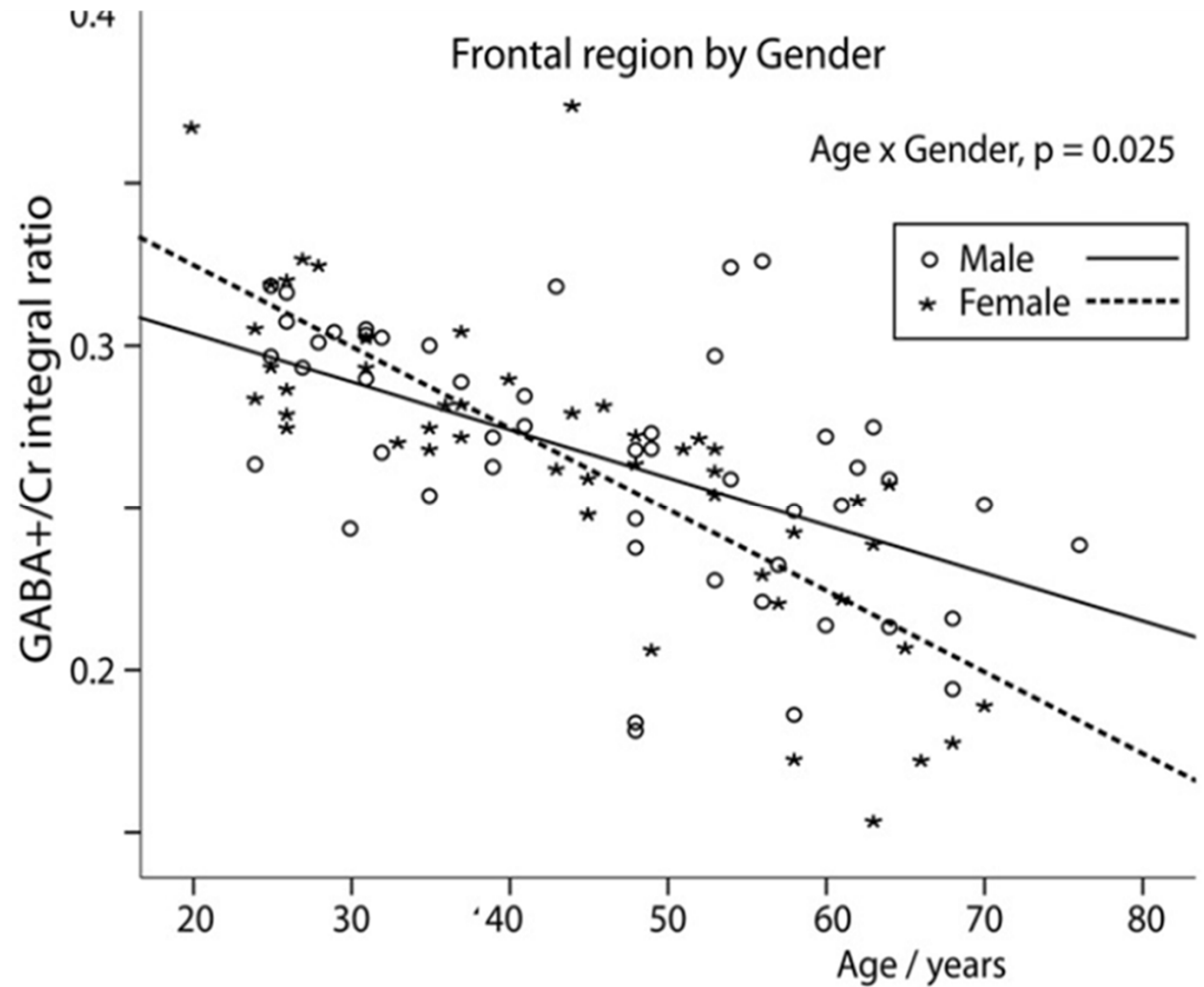
- Frontal lobes
- Executive function
- Working Memory
- Fluid Intelligence
- Theory of Mind & Perspective Taking (Piaget)
- Google Scholar (1,000s →)

	Inhibition AND
Frontal Lobe	125.0
Executive Function	113.0
Working Memory	297.0
Fluid Intelligence	21.2
Theory of Mind	41.6
Piaget	50.9

Frontal Lobe

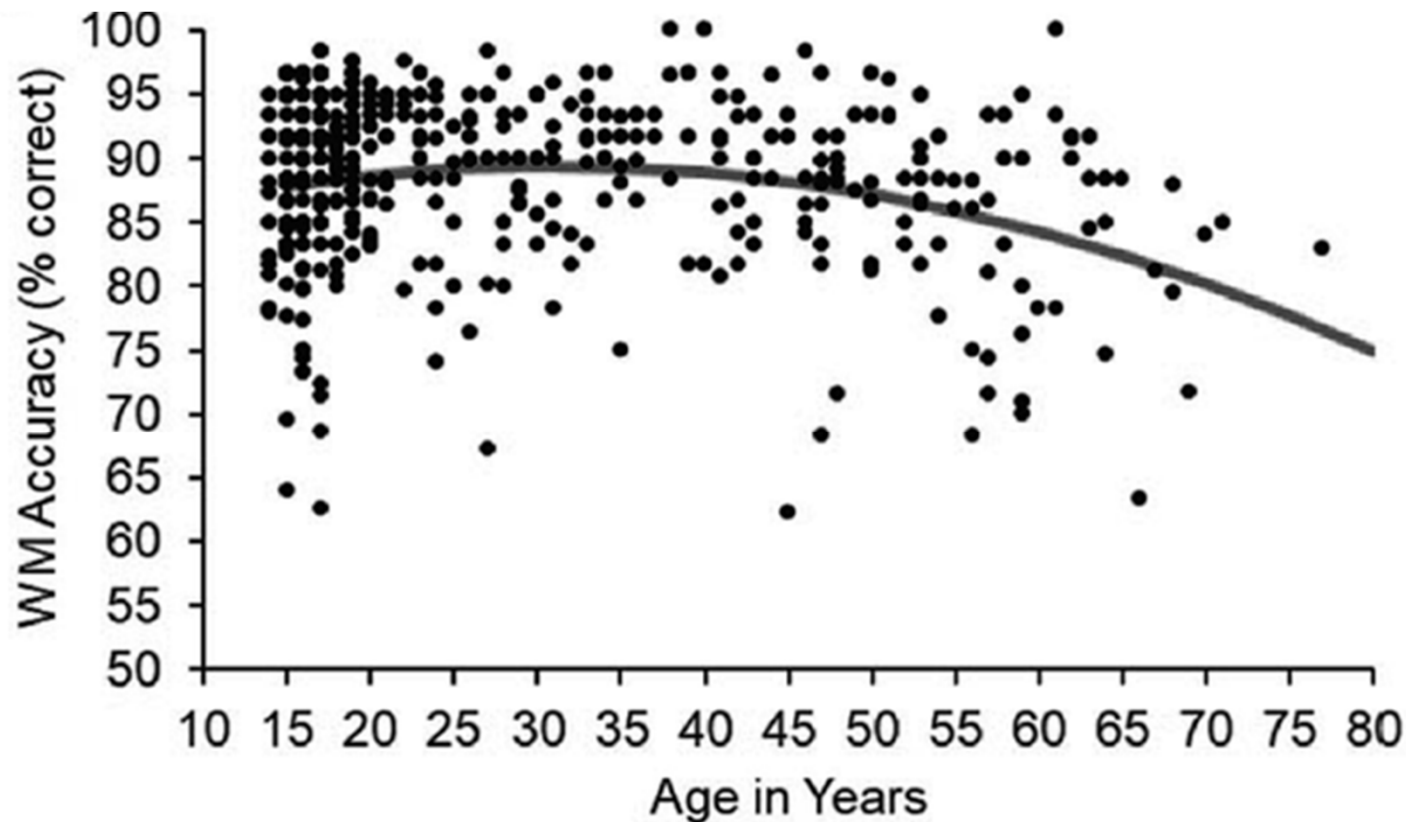
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- Decline in GABA with age (Gao et al., 2013)



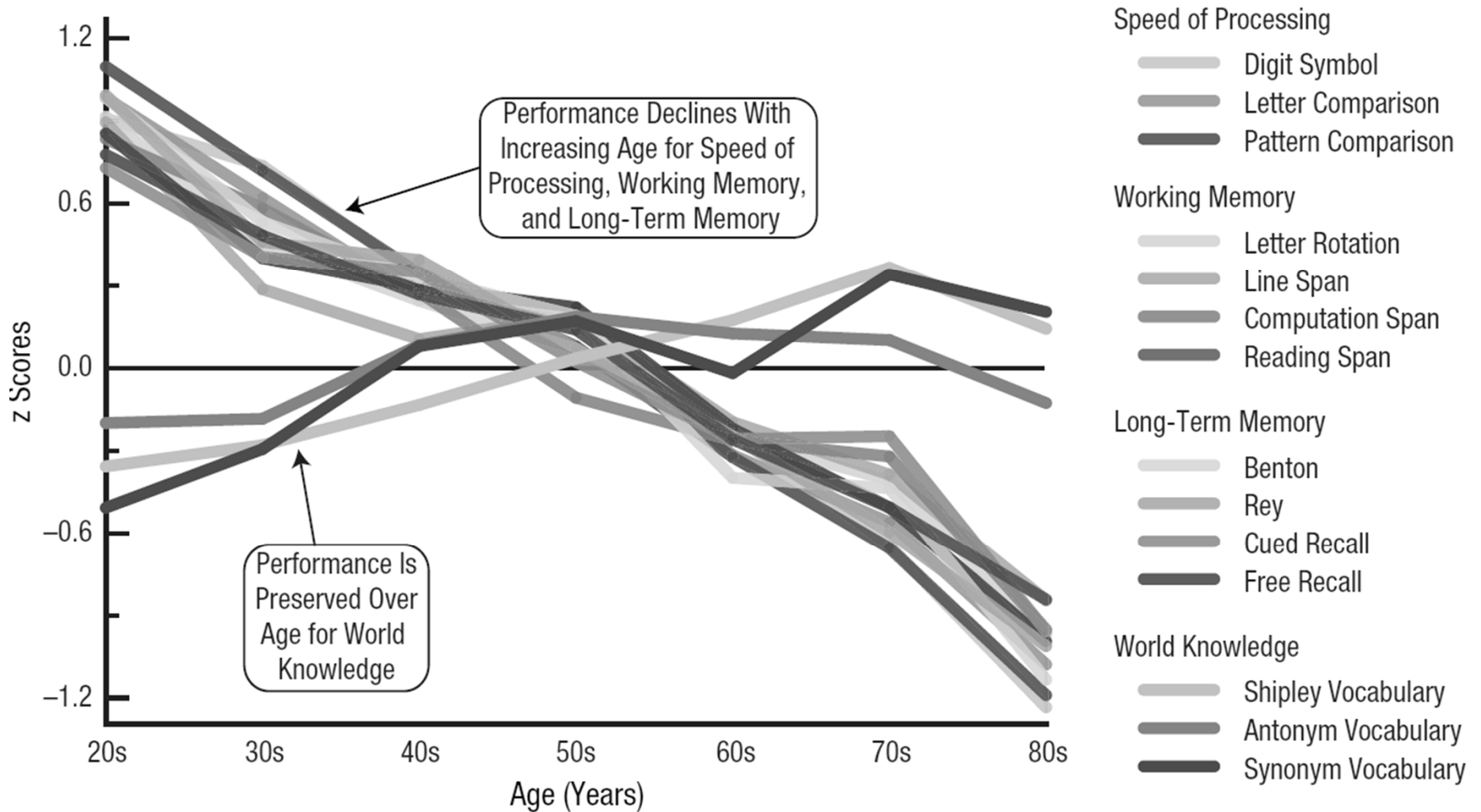
Working Memory

- System for temporary storage and manipulation of information (ZanESCO et al, 2020)
- Central role in cognitive development (Cowan, 2014)



Fluid Intelligence

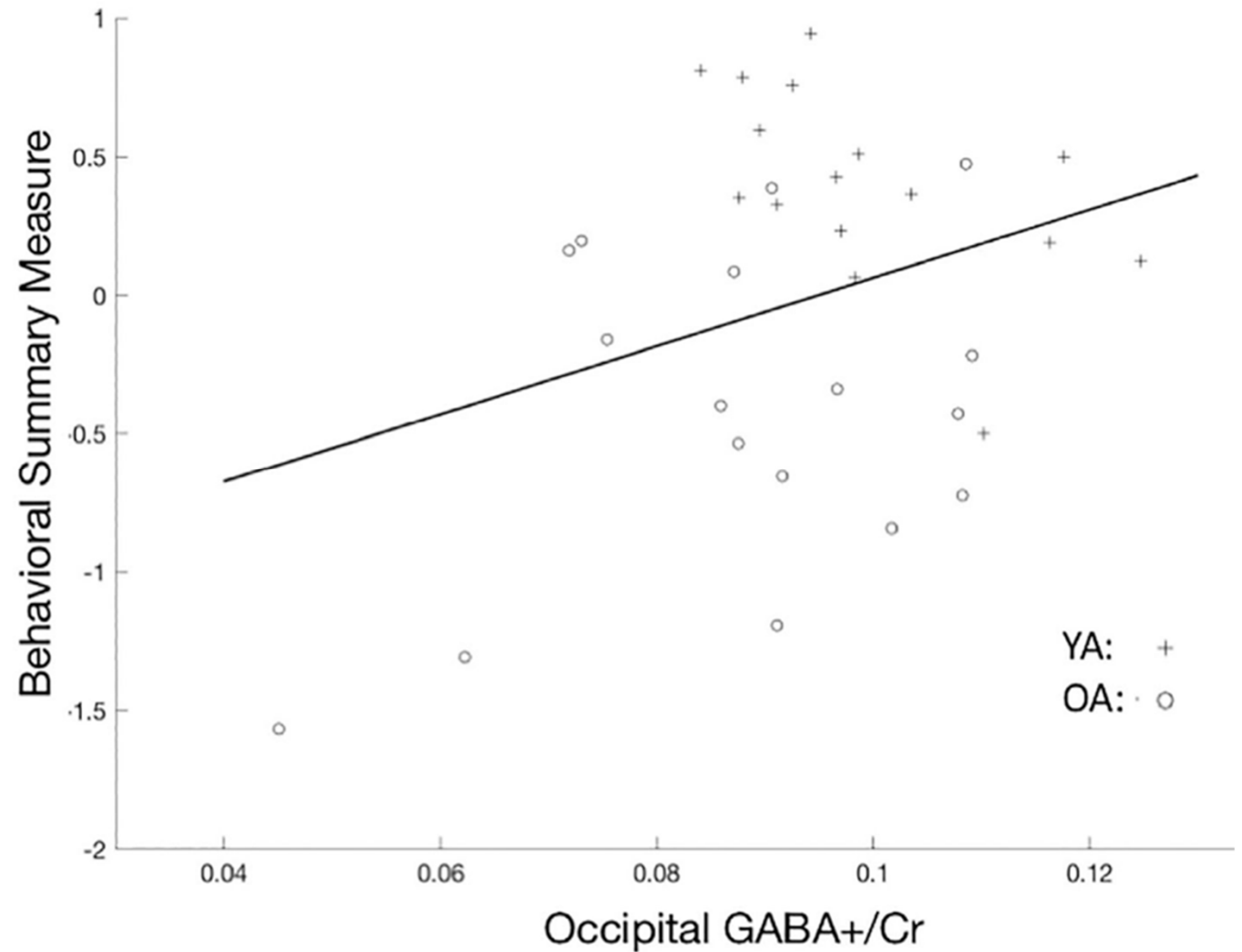
- Age (Spreng et al, 2019)



Fluid Intelligence

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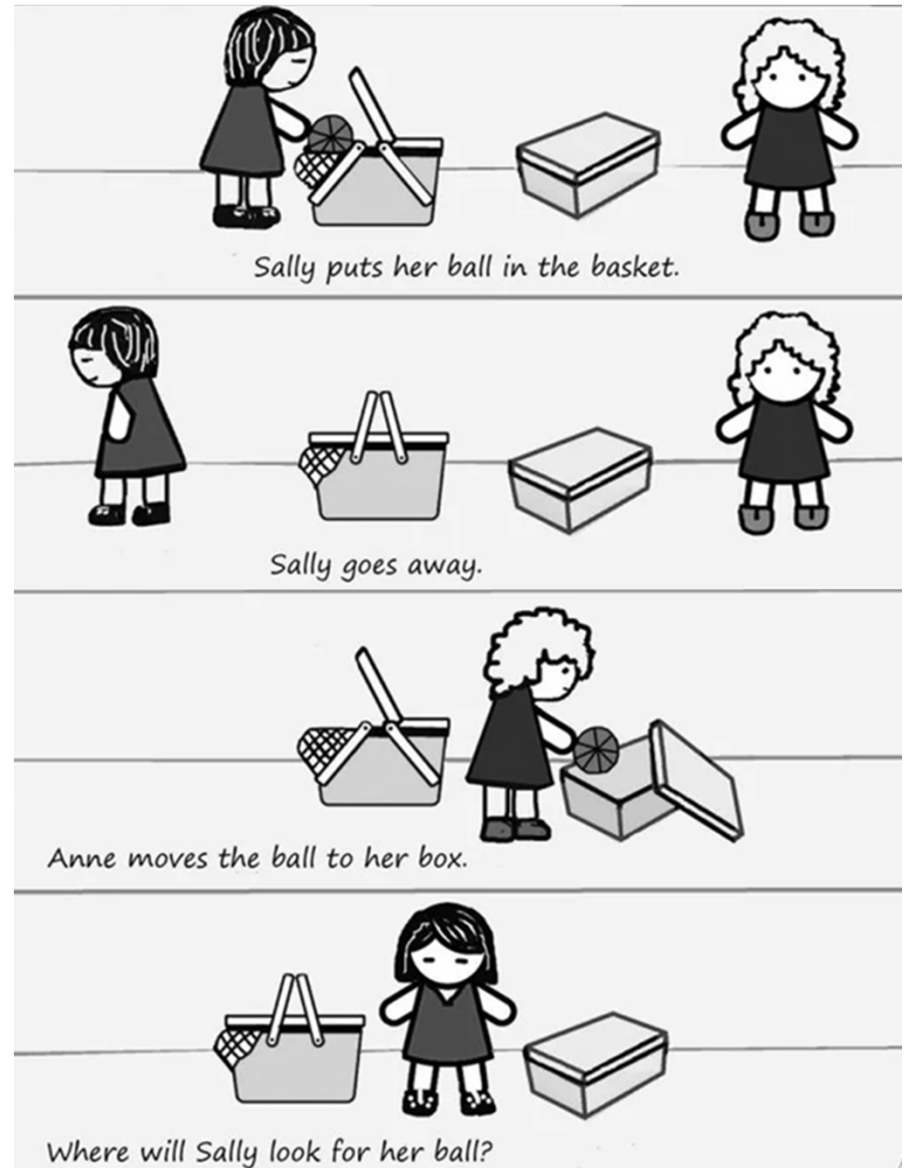
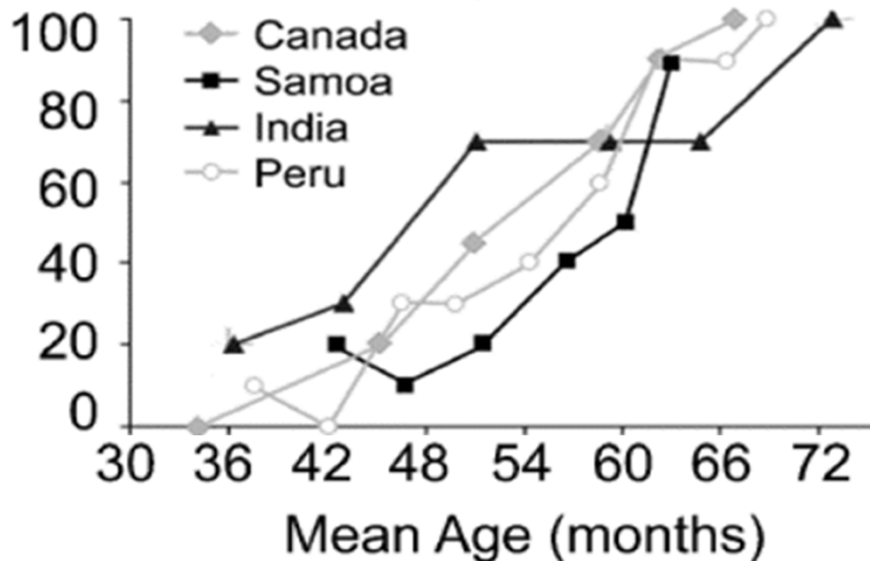
- And GABA (Simmonite et al, 2019)



Theory of Mind

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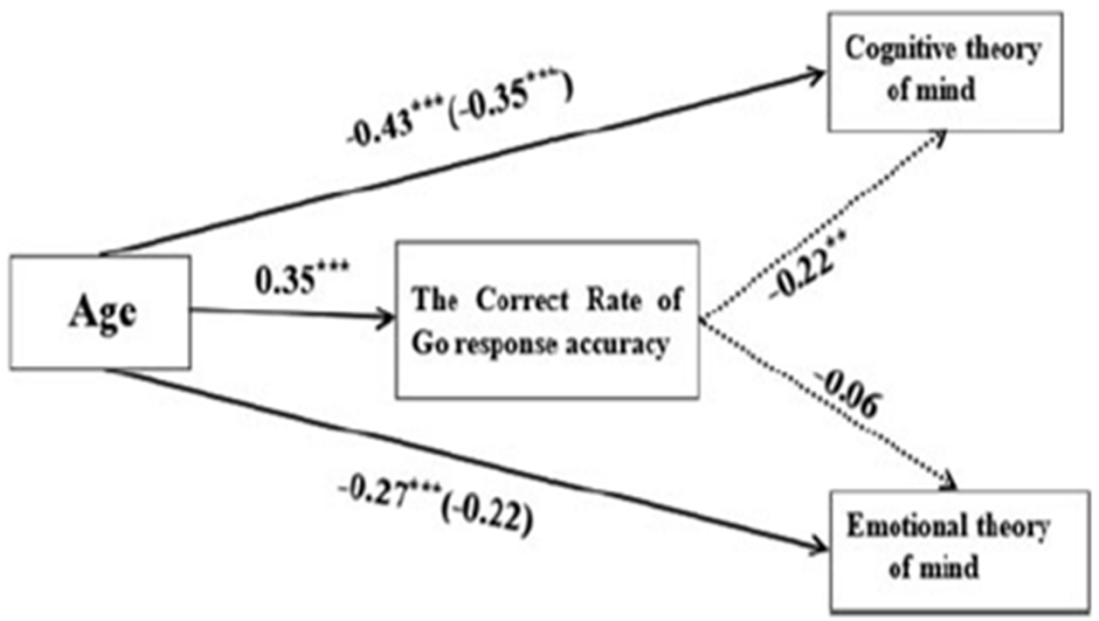
- TOM and Perspective Taking (Piaget)
- False Belief Task (right)
- Age across cultures (Callaghan et al., 2005) (below)



Theory of Mind

- TOM & Aging (Zhou et al., 2019)
- Cognitive TOM: False Belief Task (top)
- Inhibition: TOM effect mediated by Go-NoGo RT task (bottom), not Stroop

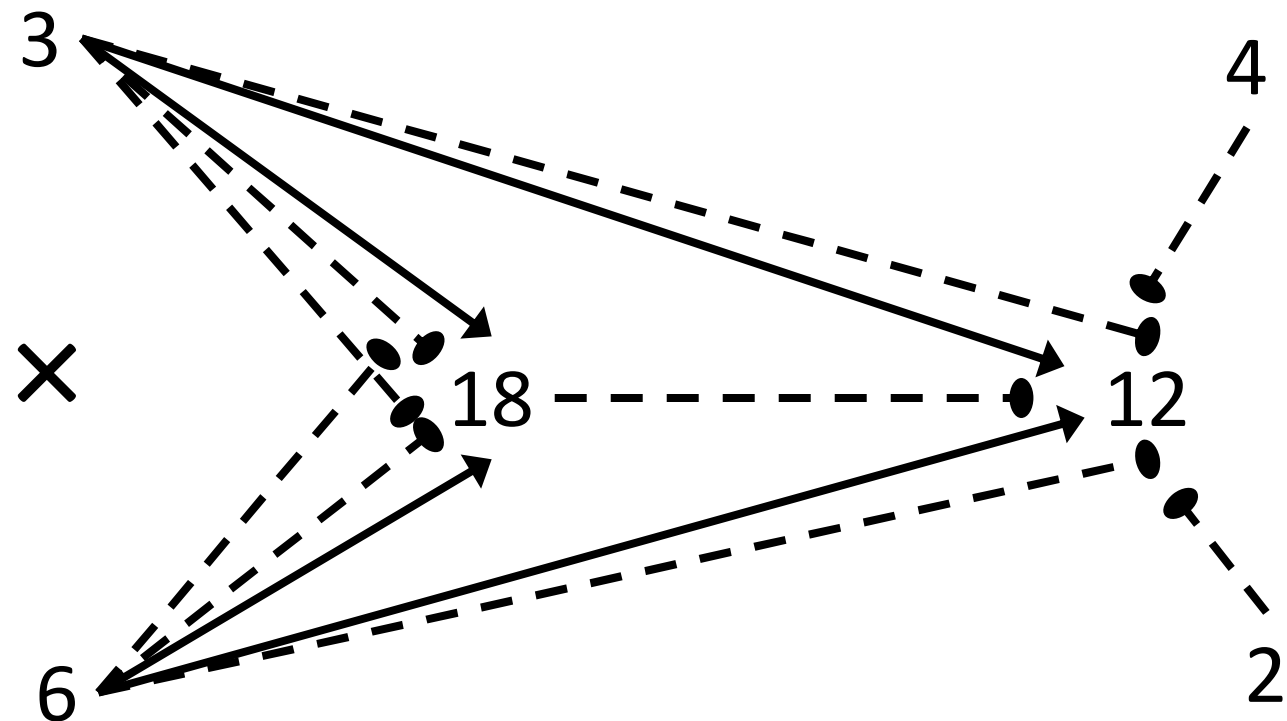
Age group	<i>M</i>
The young (<i>n</i> = 30)	0.94
65–74 (<i>n</i> = 28)	0.91
75–79 (<i>n</i> = 30)	0.75
80–84 (<i>n</i> = 28)	0.68
85–89 (<i>n</i> = 26)	0.60



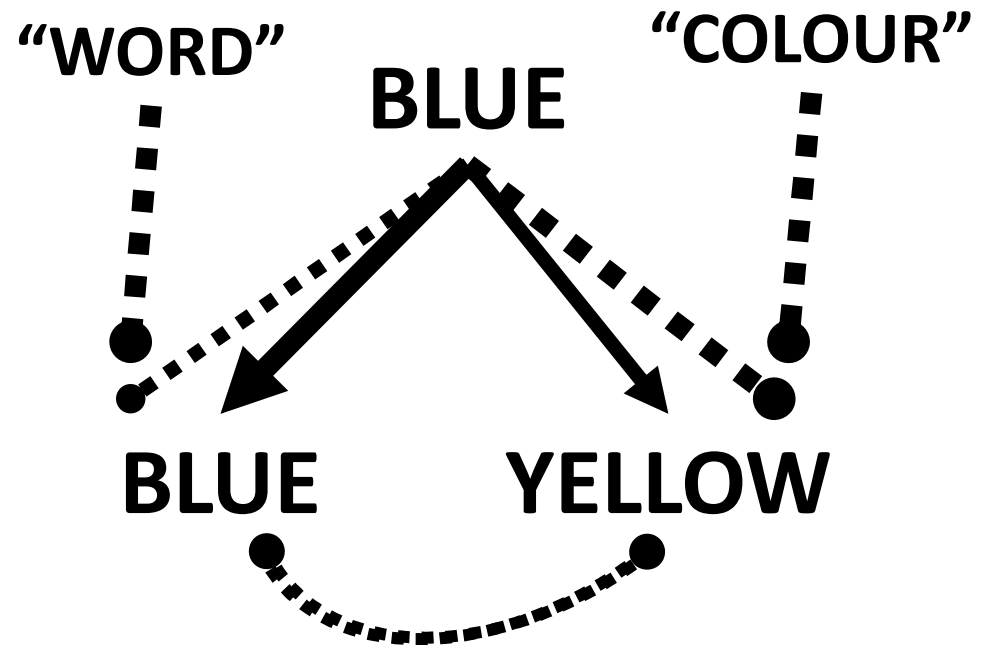
INHIBITION & MECHANISTIC MODELS

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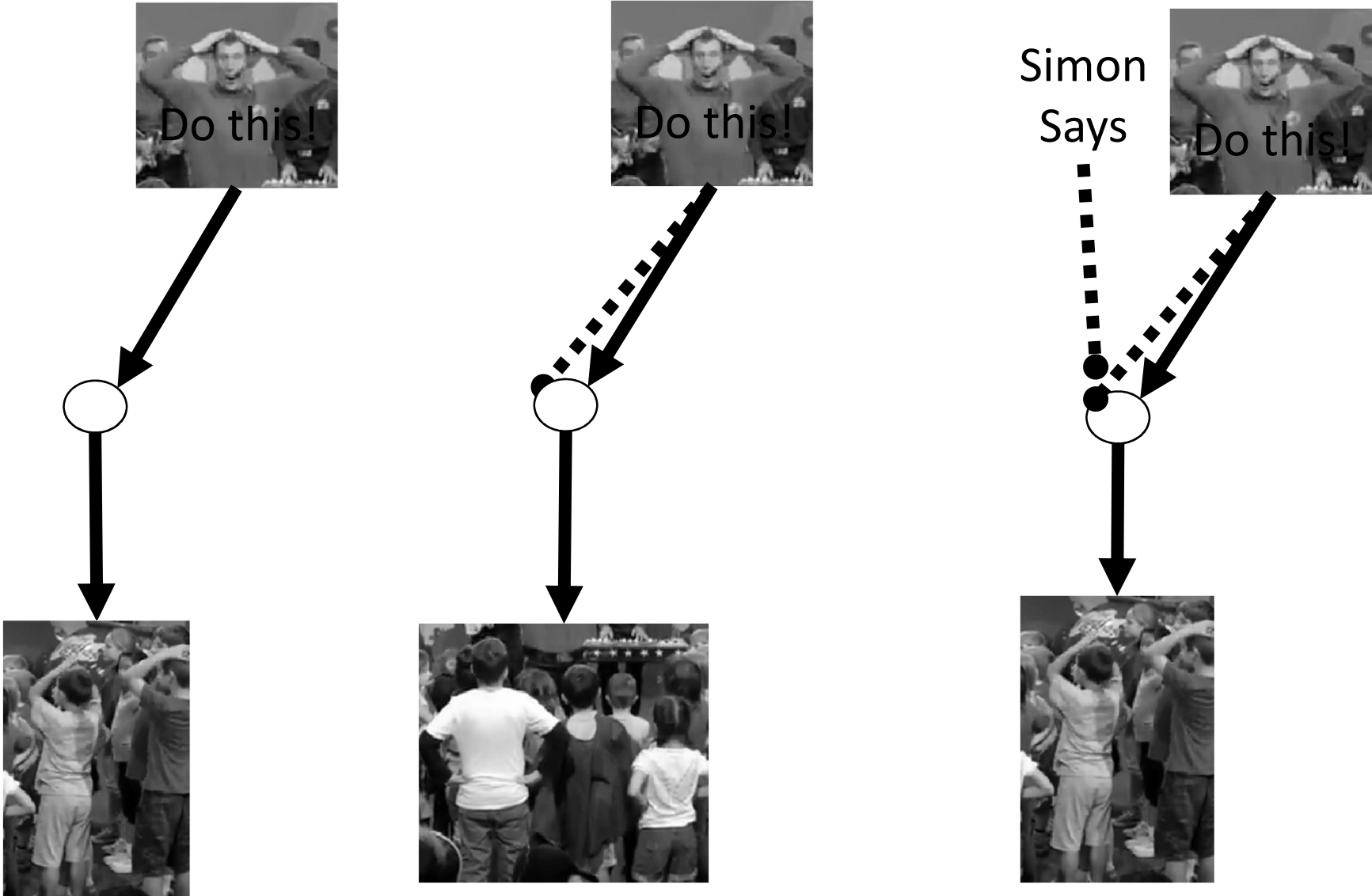
- Inhibition “explains” diverse phenomena
- Complete explanation requires mechanistic model
 - Simple inhibition works for some tasks (e.g., acuity, VEPs, ...)
 - But, ambiguous, context-dependent tasks (e.g., multiplication)



Mechanistic Model for Stroop Task

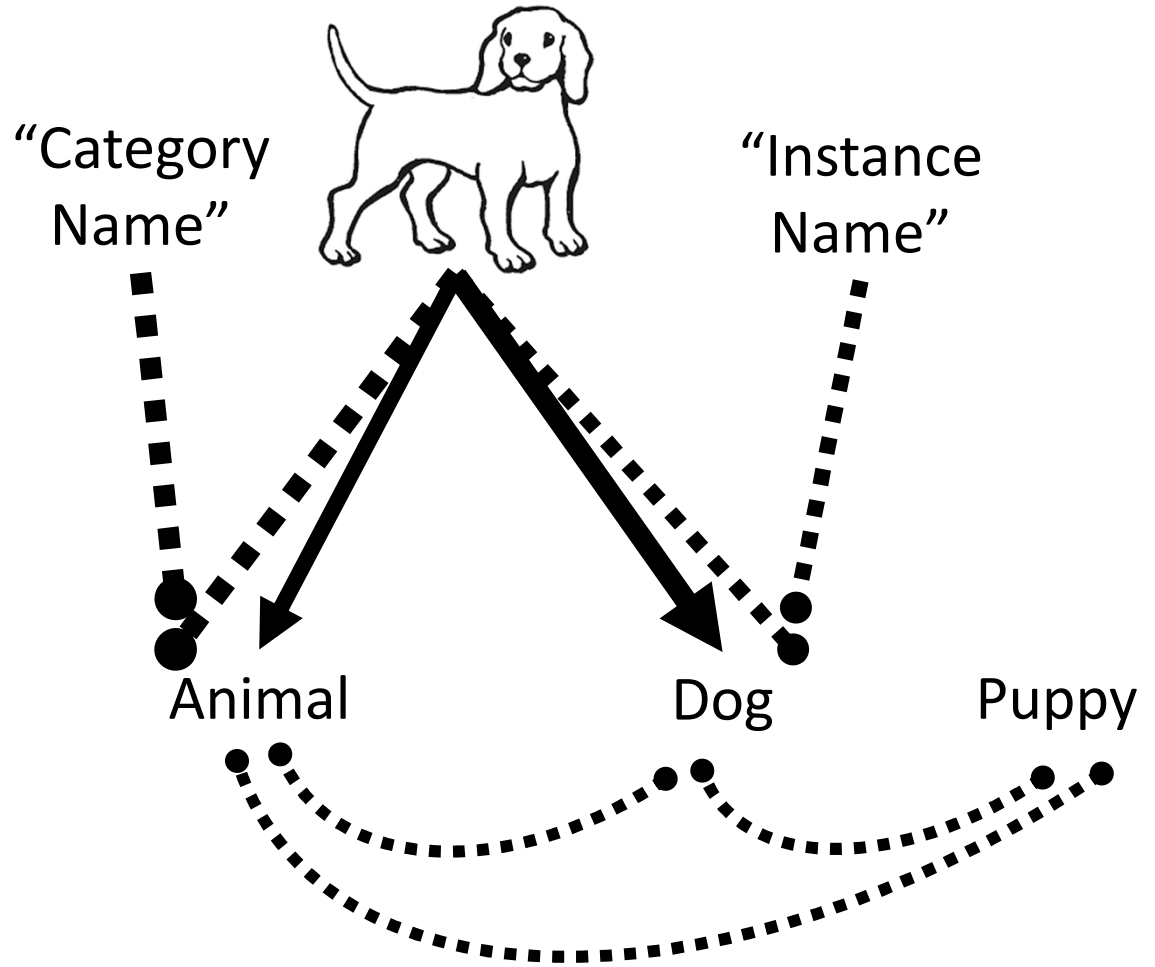


Mechanistic Model for "Simon Says"



Mechanistic Model for Naming

- Different name depending on instructions (context)

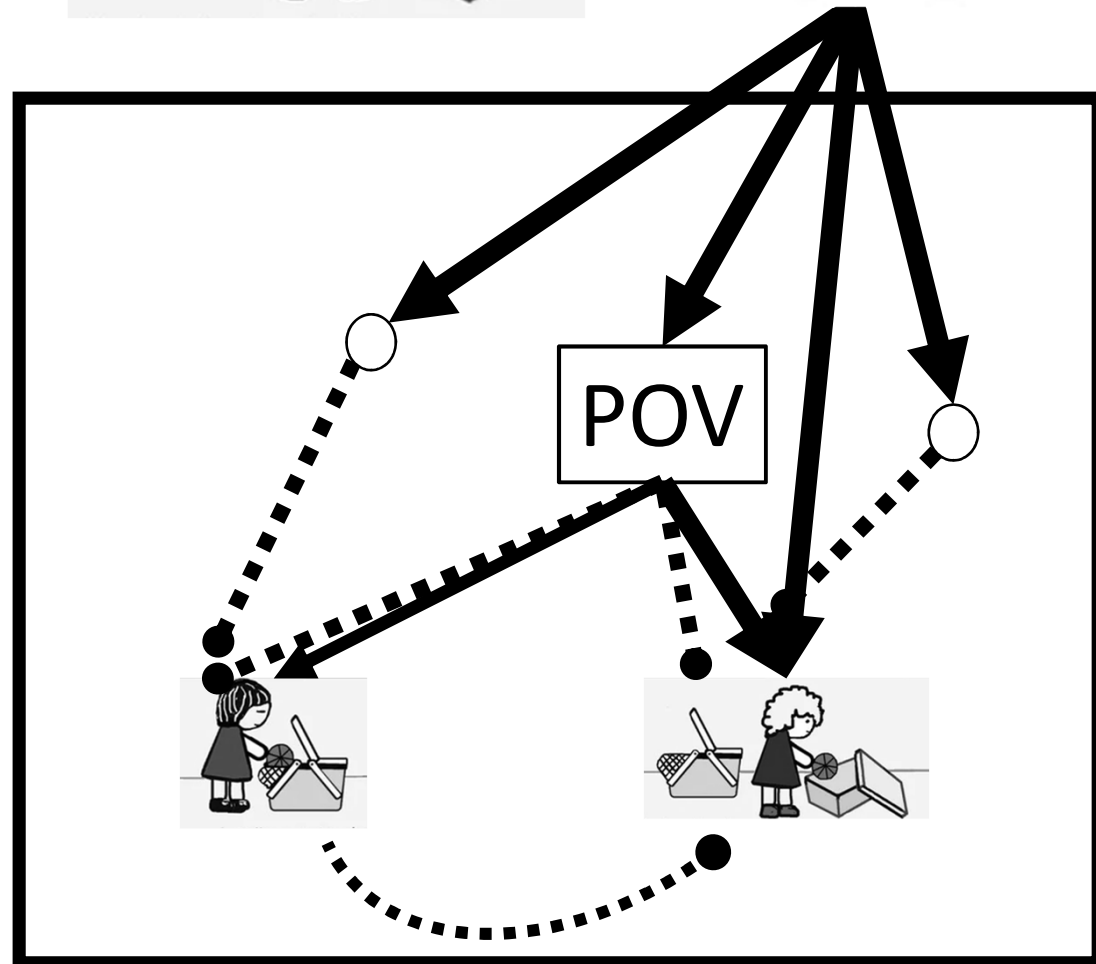


Mechanistic Model for False Belief Task

Which will Sally Chose?



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Caveats

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- Observations
 - Replication
 - Conflicting results
 - Positive Effects of Weak Inhibition
- Theoretical
 - Definition of inhibition
 - Specification of competing theories
 - Origins of increase and decrease with age
- Is it plausible that single mechanism can underlie such diverse results?
 - Google Scholar (1,000s →)

	Inhibition AND
Age	5,370
Aging	3,090
Childhood	2,060
Children	3,740
Perception	2,920
Attention	4,880
Memory	3,520
Language	3,450

Thanks for Listening!

Questions? ... later

j.clark@uwinnipeg.ca