JOHNS HOPKINS
SCHOOL of MEDICINE

DIVISION OF COGNITIVE NEUROLOGY / NEUROPSYCHOLOGY
DEPARTMENT OF NEUROLOGY

Maximal Mental Exercise: Promoting Speech and Sociability in a Nonverbal Individual with Autism

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October 28, 2021

Please Note

- To help ensure anonymity, this presentation will not be video recorded.
- Slides from this talk (redacted) are at http://web.jhu.edu/cognitiveneurology
- Don't hesitate contacting me at:
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Overview

- Translational medicine (precision medicine, personalized medicine)
  - 8-year-old male with autism, nonverbal, with severe intellectual disability
  - Prognosis for such individuals has been poor
  - What could be done – *drawing on any and all fields of knowledge, specialties, and methods for intervention* – to improve his capabilities?
    - Cognitive neurosciences (cognitive science, neuropsychology)?
    - Neuropathology?
    - Pharmacology?
    - Brain stimulation approaches (e.g., tDCS and TMS)?
    - Behavioral methods ("teaching")?
  - Using behavioral methods corroborated by the cognitive neurosciences – *individualized, intensive behavioral methods informed by ongoing data* – there have been considerable improvements in his behavior, speech, and ability to learn.
  - ~21 years: basic neurobiology X his condition
  - Distinct possibility that even higher goals are feasible for him and for others

Autism Spectrum Disorder (ASD)
General Background

- Currently, diagnosis purely behavioral
- Behaviors described for > 500 years (Lord et al., 2020); first described formally by Kanner, 1943 (but see Chown & Hughes, 2016)
- Varied definitions applied to varied conditions over the years.
- Current clinical definition: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM 5* (APA, 2013)
  - "Persistent deficits in social communication and social interaction across multiple contexts..."
  - "Restricted, repetitive patterns of behavior, interests, or activities..."
  - "Symptoms must be present in the early developmental period (but may not become fully manifest [until later])…"
- Many other concurrent issues (e.g., anxiety, resistance to change)
- TBD: Splinter skills – savant skills

Autism Spectrum Disorder (ASD) General Background

- Can be diagnosed in other conditions (syndromic ASD; e.g., RETT syndrome, fragile-X)
- Idiopathic, nonsyndromic ASD is the focus in this talk.
- Prevalence: 18.5/1000 (1:54) among 8-year-old children (CDC; Maenner et al., 2020)
- Presentation: ~70% persistent developmental delays, ~30% regressive
- Male-to-female ratio: ~4-5:1

Autism Spectrum Disorder (ASD) General Background

- ~100 genes known to be associated (e.g., Iakoucheva et al., 2019; Woodbury-Smith et al., 2018)
  - Inherited as well as *de novo* mutations
  - Regulatory functions, energy metabolism, synaptic modeling, etc.
- Estimated that ~500-1000 genes involved in idiopathic autism (Lord et al., 2020)
- "Subtle" differences on neuropathology, structural, and functional imaging (Lord et al., 2020)
  - Possible lower intraepidermal nerve fiber density (Chien et al., 2020)
- Clinical presentation is thought to be the culmination of developmental and environmental domino effects, complexly interacting over time (e.g., Johnson et al., 2017) (cf. congenital blindness).

Autism Spectrum Disorder
Heterogeneity of the Condition

- Seems fairly clear now there are considerable behavioral, genetic, and probably neurobiologic differences among individuals within the broad category of ASD, although categorization is very controversial.
- One consequence: findings from one group may not be applicable to another.
- For current purposes, distinguish a subgroup of ASD with severe intellectual impairments (low-functioning autism, severe autism [National Committee for Severe Autism]; within ASD-level 3 by DSM-5 criteria).

ASD with Severe Intellectual Impairments

- A.I.'s category: Nonverbal with severe intellectual disabilities
- Relatively little investigation of the neurobiology or the potential treatment of such individuals (At one recent meeting devoted to autism, only 4% of the papers were concerned with such individuals.)
- Barriers to investigation include: Very limited abilities; behavior extremely variable; very difficult to get cooperation; potential for physical aggressiveness
- Large number of mainstream and not-so-mainstream therapeutic (teaching) efforts
  - E.g., discrete trial; pivotal response therapy
- Prognosis "poor"
  - E.g., for speech: Widely cited clinical rule of thumb at the time: If an individual has not developed speech by the age of 5, it is 'very unlikely' that s/he will ever develop oral speech.
  - Review by Pickett et al. (2009) confirmed it was very rare for a nonverbal individual with autism to acquire speech after the age of 5.

Initial Goals of the Educational Program

- Which skills to develop in A.I.?
  - Communication system – for behavioral management (e.g., A.I.'s wishes), teaching, interactions with family and other people

Which Communication System?

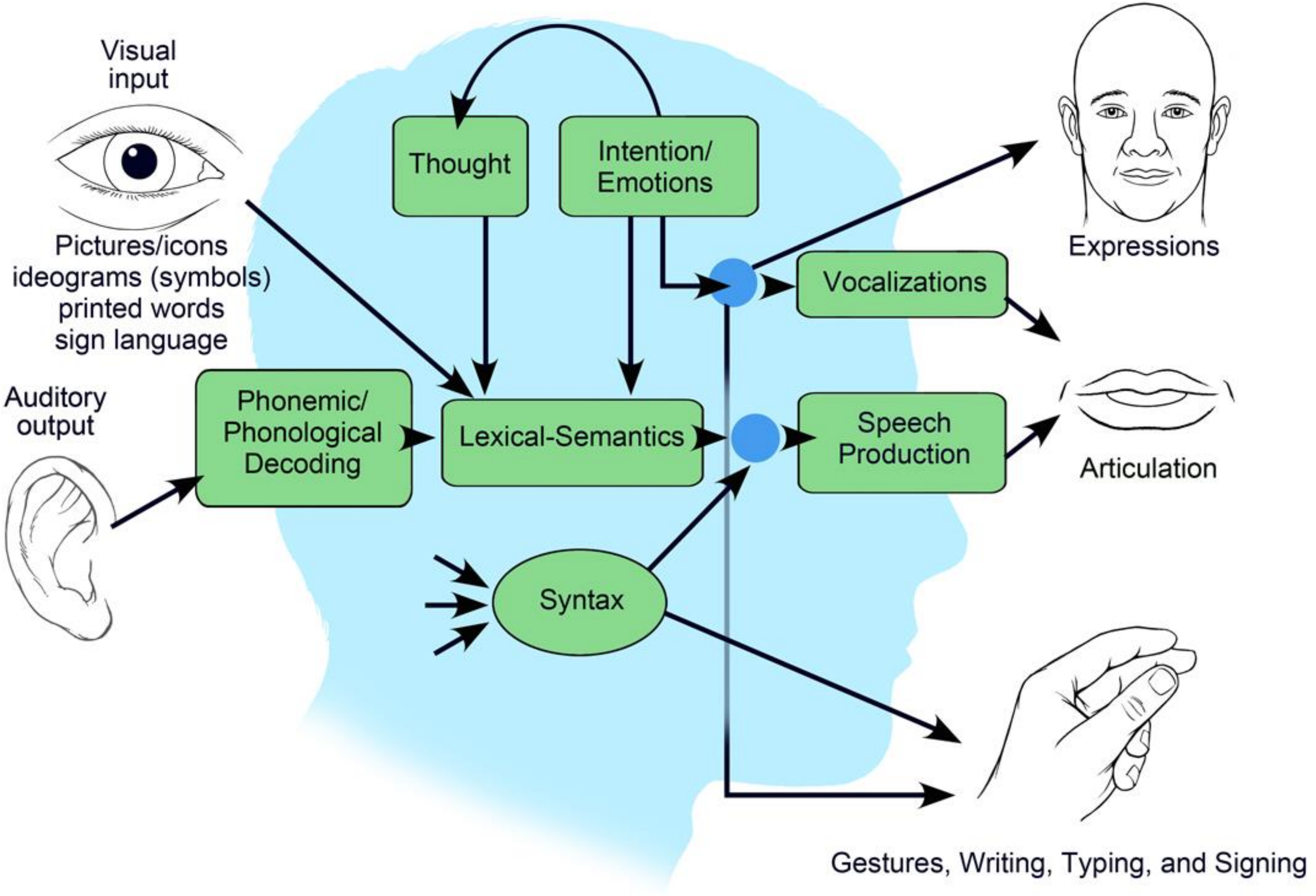
- Board or device with photos/line drawings/symbols?
- Sign language?
- Oral speech?
  - If feasible, most readily available
  - Easiest to use with others (oral speakers)
  - Ultimately, most expandable
  - Bridge to reading, writing

Speech Is More Than Communication

- It has been speculated that oral speech evolved not just as an aide to communication, but because it can aid thinking.
  - More persistent memory (auditory-verbal working memory), abstraction, etc. (cf. Bickerton, 1990)
  - The resulting feedback loop led to an explosive growth in the abilities of human thought as well as speech → language.
- Giving A.I. oral speech may give him mental tools for better thought processes.

What is Required for Speech?

Auditory and Visual language User

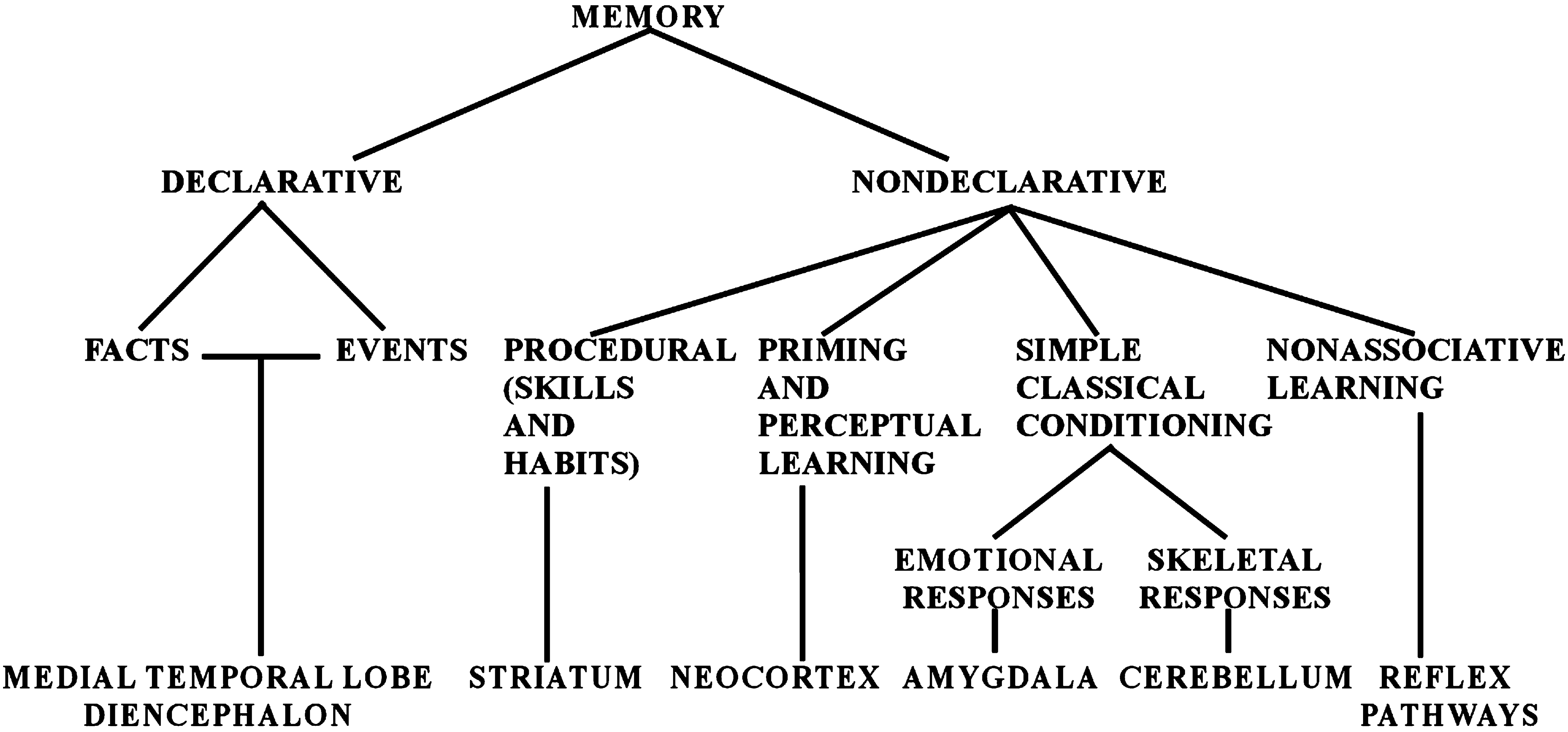


What is Required for Speech?

- Speech production
  - Articulation
    - Motor skill
    - Extremely demanding motor skill
      - Coordination of respiration, larynx, soft palate, tongue, jaw, and lips
      - High speed

How Can Speech Production be Learned?

- Memory (learning) ‘classically’ divided into
  - Declarative memory (learning)
  - Non-declarative (procedural) memory (learning)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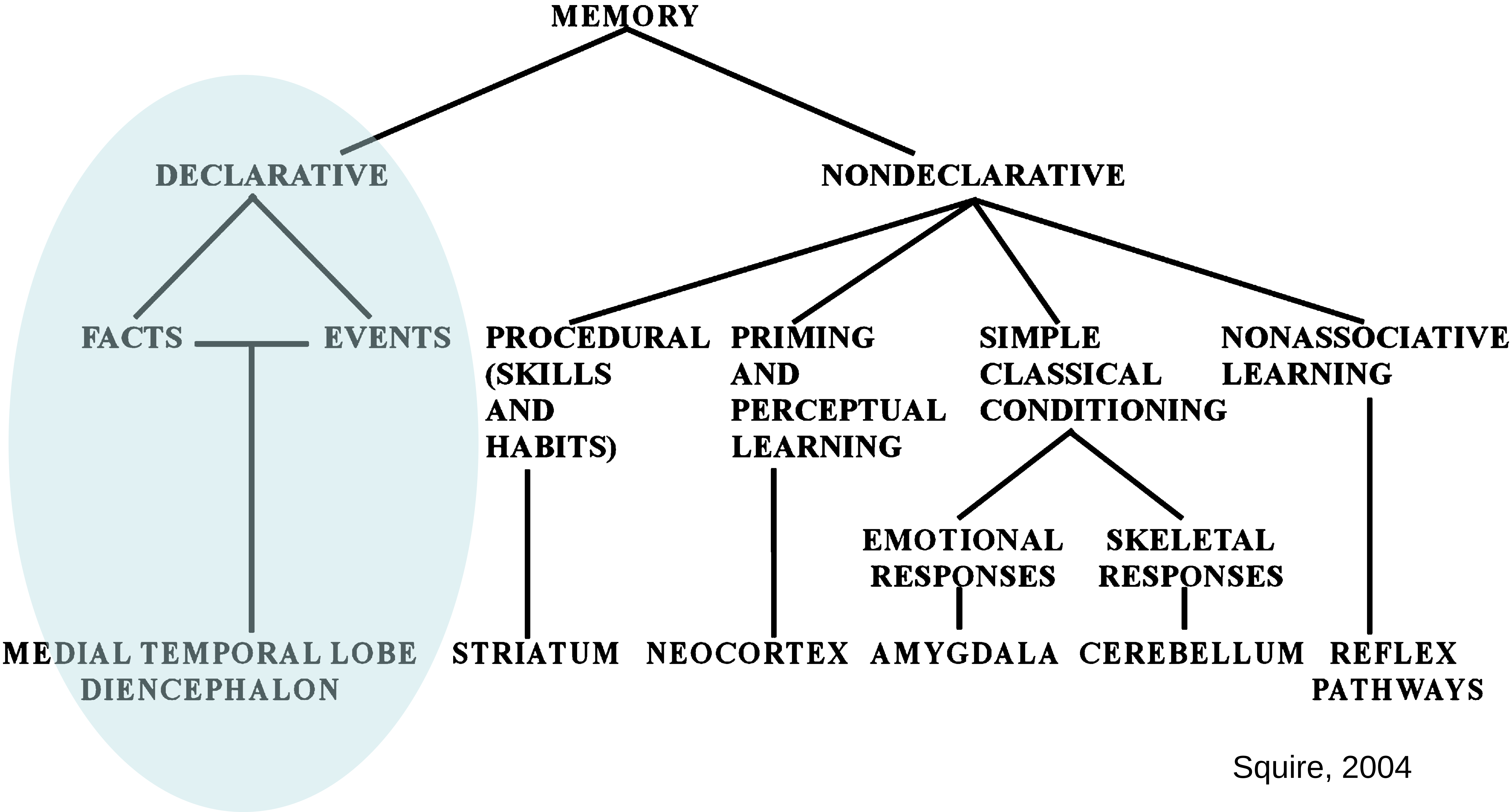
FACTS
EVENTS
PROCEDURAL (SKILLS AND HABITS)
PRIMING AND PERCEPTUAL LEARNING
SIMPLE CLASSICAL CONDITIONING
NONASSOCIATIVE LEARNING
EMOTIONAL RESPONSES
SKELETAL RESPONSES
MEDIAL TEMPORAL LOBE DIENCEPHALON
STRIATUM
NEOCORTEX
AMYGDALA
CEREBELLUM
REFLEX PATHWAYS

Squire, 2004

Declarative Learning

- Clinical testing of memory and learning is heavily a test of declarative knowledge and learning.
  - E.g.,
    - Episodic memory (What were the words I asked you to remember a few minutes ago?)
    - Factual knowledge (What structures are in the medial temporal lobes? Name all the Islands of Langerhans.)
  - Learning can be very rapid.
  - Language is intimately involved in much of what is tested.
  - Critical role for the hippocampal/medial temporal system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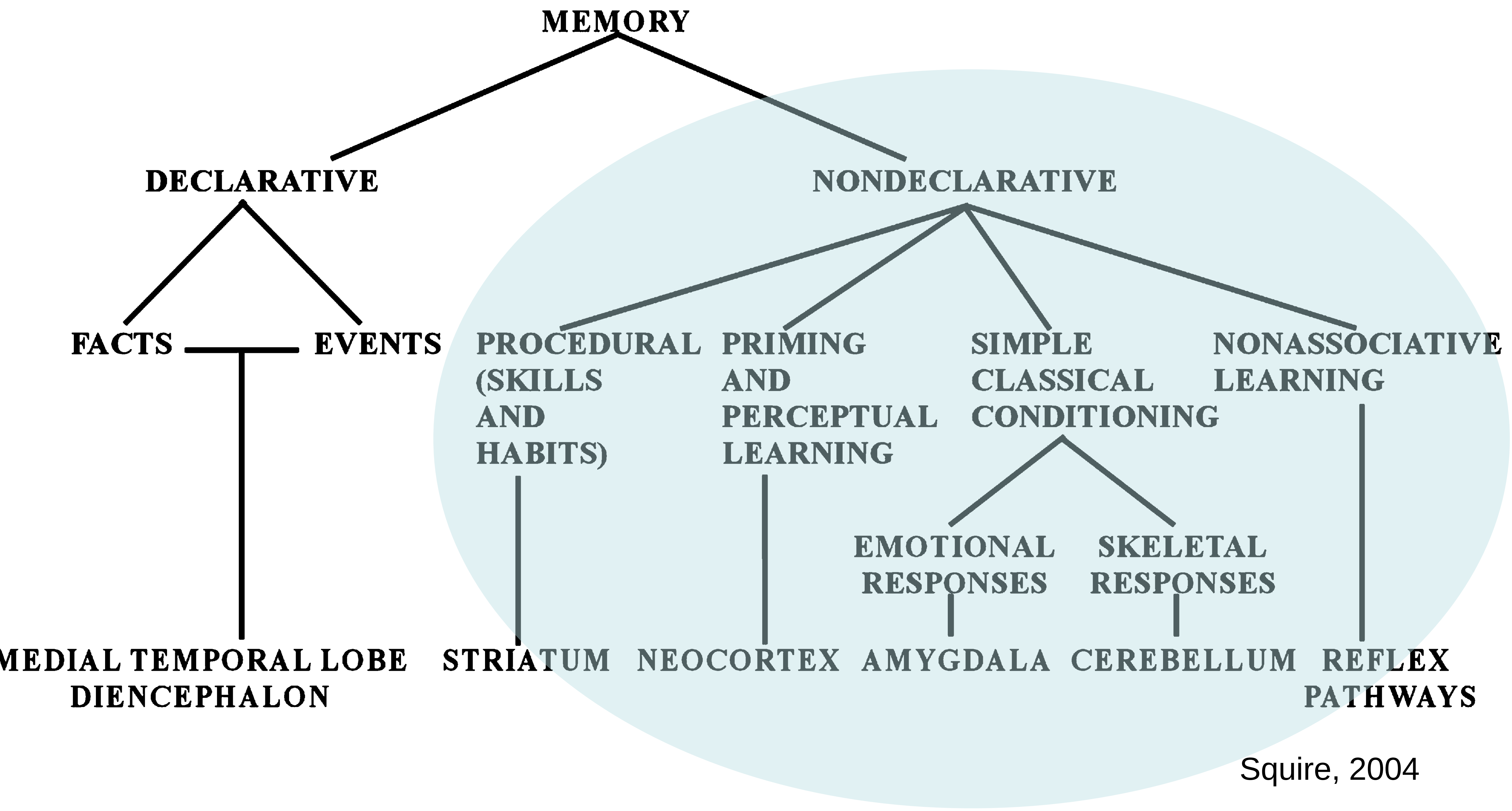
How Can Speech Production be Learned?

- There is general agreement that speech production is learned as a skill; it is not declarative learning.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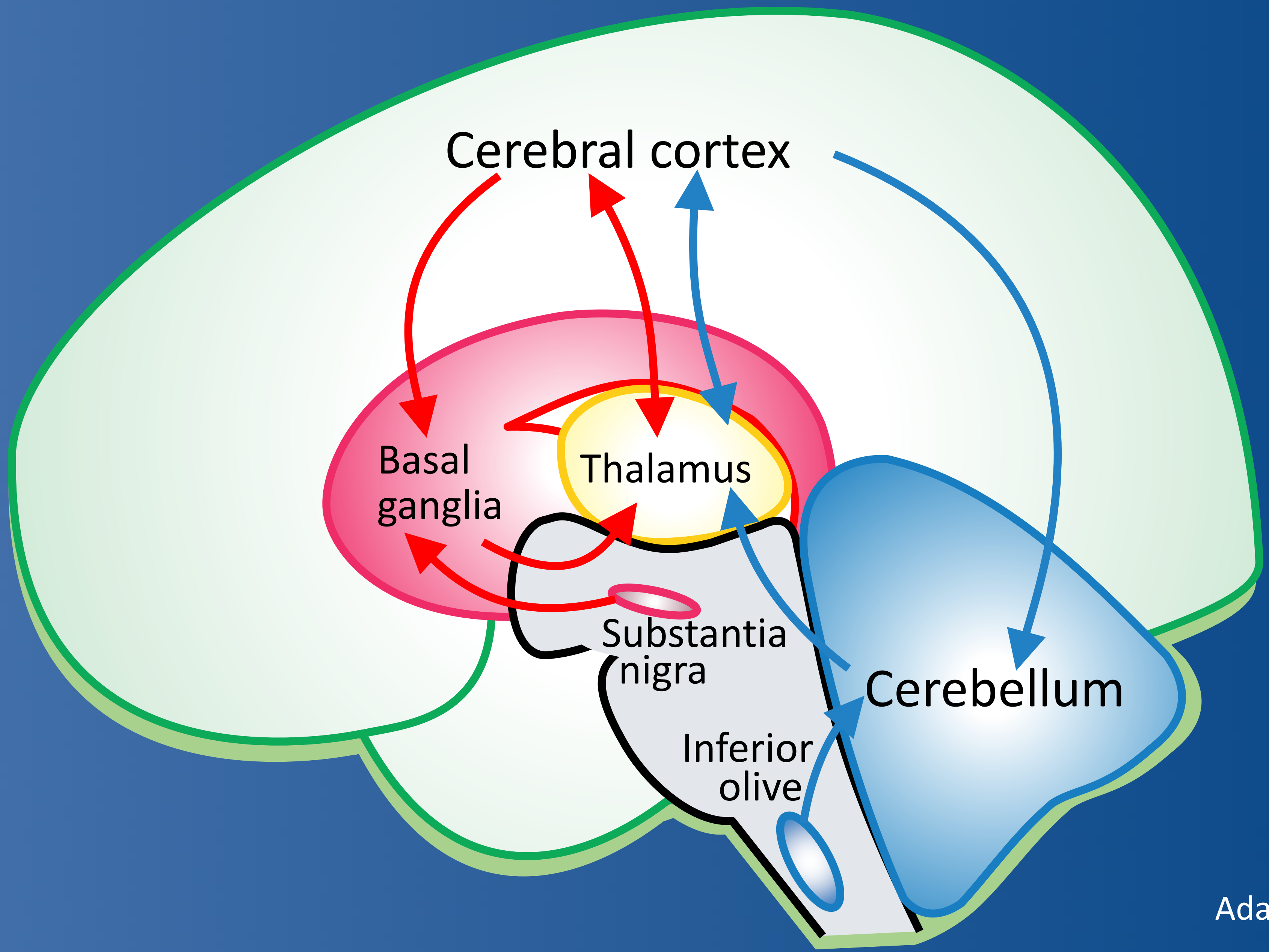
Skill Learning

- Traditional examples: riding a bike, driving a car, learning golf or tennis
- Not dependent upon language (although can be directed via language)
- Learned by performing
- Typically, learning is slow, requiring many repetitions.
- Performance of a learned skill can be extremely rapid.
- Striatum traditional critical structure, other structures critical as well



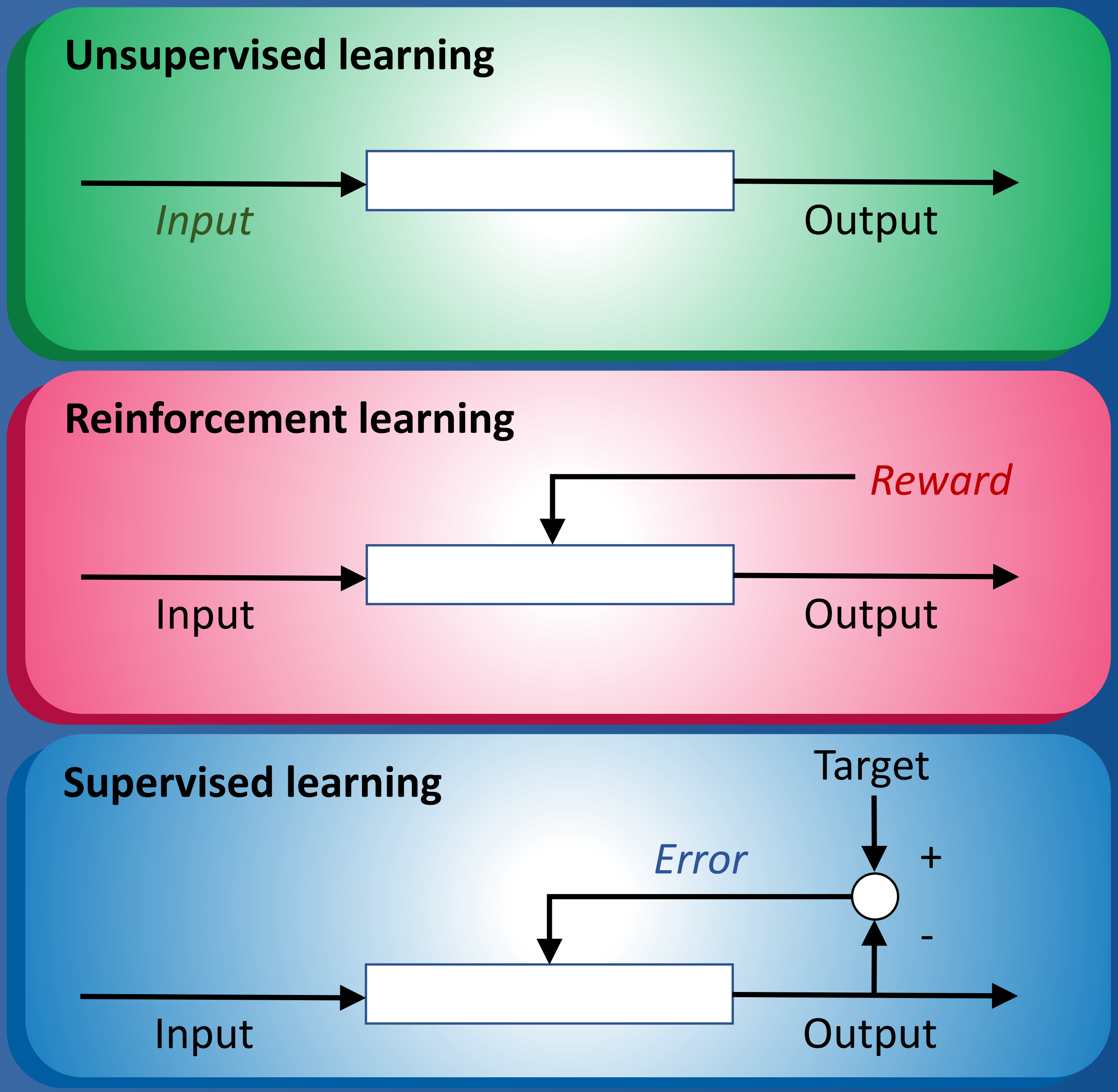
Adapted from Doya, 2000

Impediments to Learning the Skill of Articulation in A.I. and Others

- Evidence for a variety of abnormalities of basic motor function
  - Often difficulties chewing or swallowing
  - Difficulties imitating motor movements, voluntary control of respiration
- Evidence for auditory speech perceptual problems as well
  - E.g., don’t orient to sounds or to meaningful words such as their own names

Skill Learning

- There is increasing theoretical and neurobiologic knowledge of what is required for learning (skills and others).
  - Some basic mechanisms seem clear.



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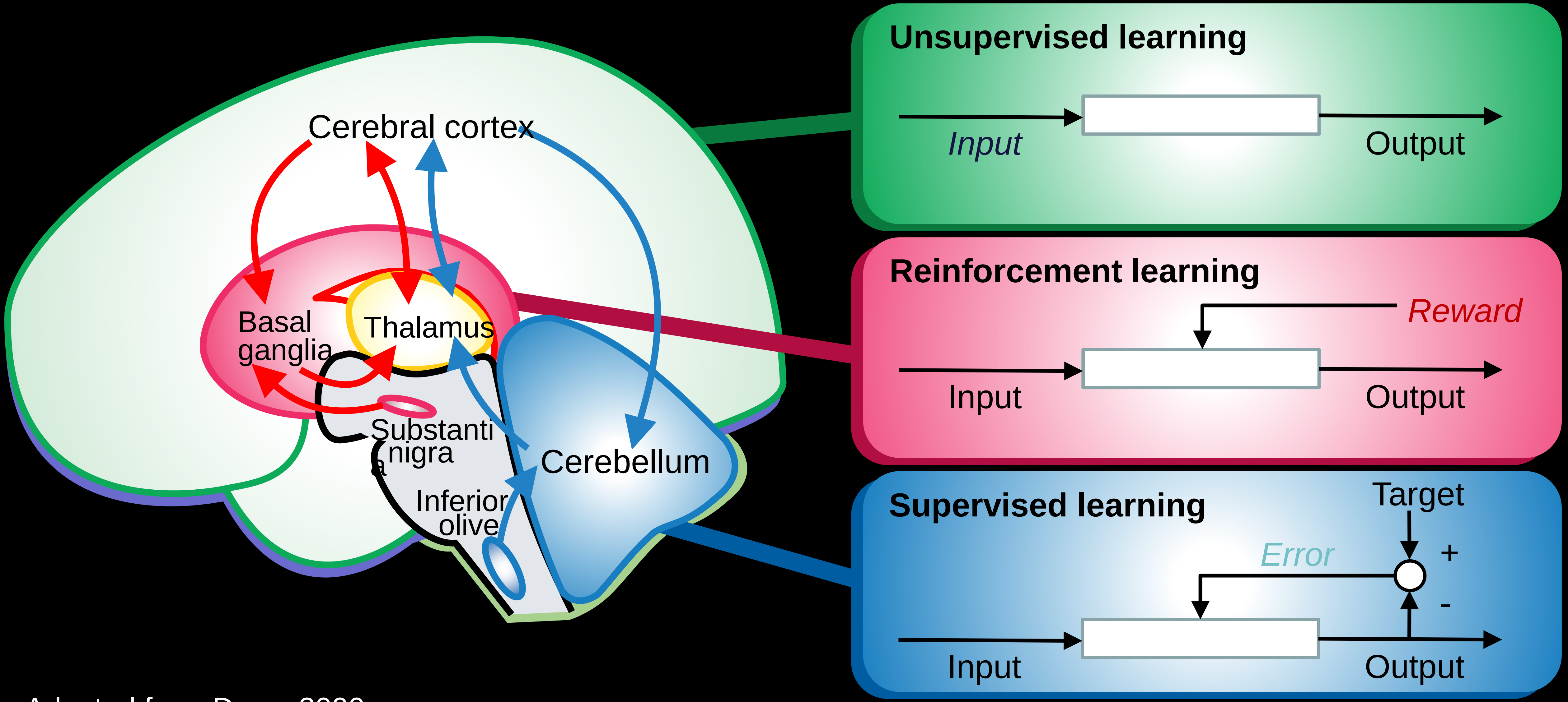


Adapted from Doya, 2000

Can the Basic Science/Neurobiology be Translated?

- Only very tentatively
  - No strong consensus as to the mechanisms operating in typically developing individuals in real-life situations
  - Only coarse, uncertain evidence as to what is and is not operating properly in ASD with severe intellectual disabilities
    - Procedural learning does seem to be intact in many paradigms in individuals with ASD, so one foundation for skill learning is relatively intact. Possible basis for savant-like skills.

Preconditions for Skill Learning

- Much better consensus as to the empirical conditions required in practice to engage the mechanisms responsible for skill learning (whatever those mechanisms are!). Examined in at least several situations:
  - Perfecting a motor skill (e.g., sports, performing arts, surgery)
  - Reacquiring a motor skill (e.g., post-stroke paresis)
  - Learning a motor skill *de novo*

Example: Post-Stroke Paresis

- Adults > 1 year post stroke, severe upper limb impairments (Daly et al., 2019; McCabe et al., 2015; see also Krakauer et al., 2021)
- Methods:
  - Broke down movements for training: Single-joint -> 2-joint -> task components -> full task
  - Trained for “quality” (proper form)
  - High-intensity: 5-6 hours/day, 5 days/week, 12 weeks
- Results:
  - Clinically significant improvements

Optimal Conditions for Learning a Skill

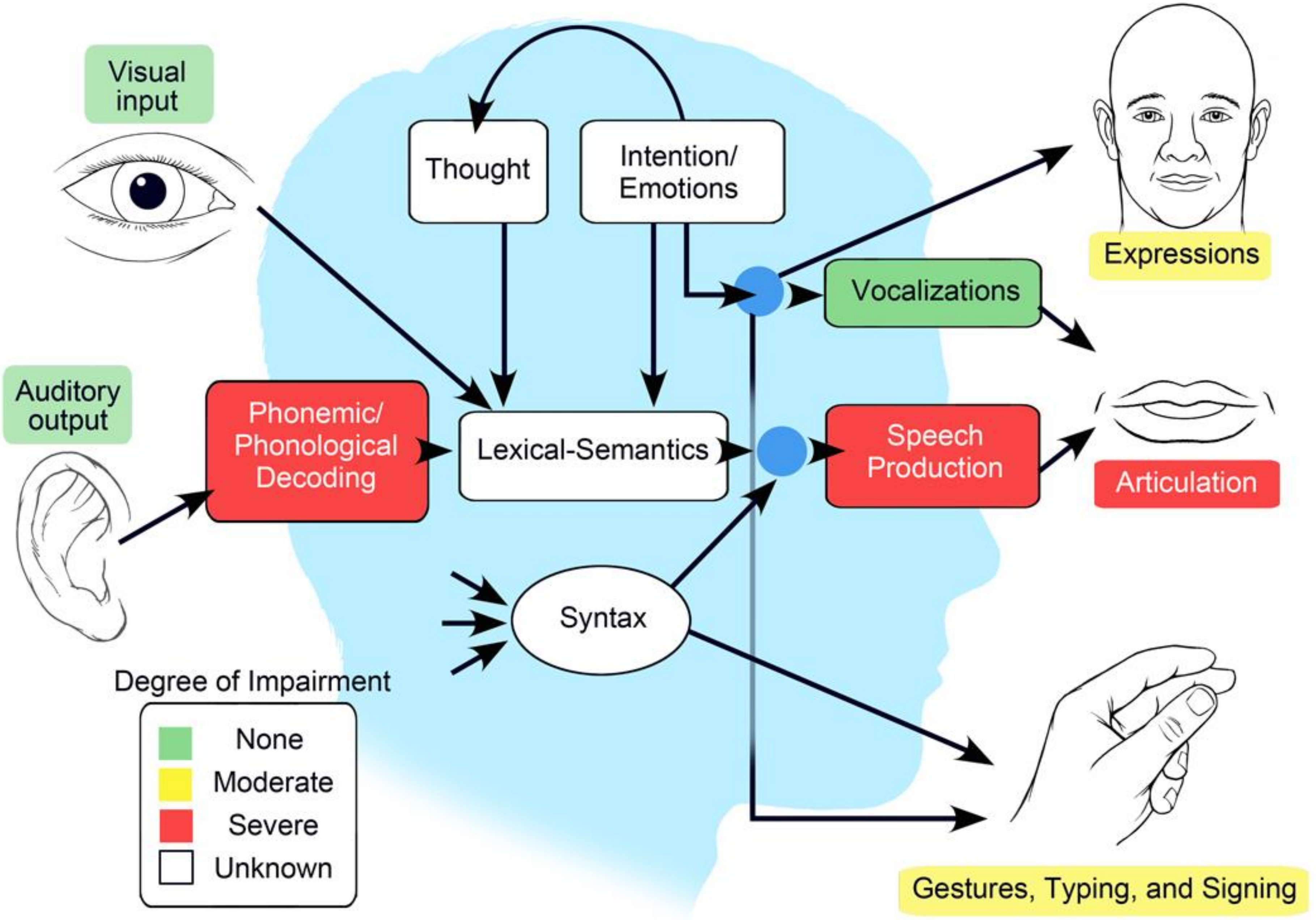
- Perform the precise skill required.
  - Maybe in some cases closely related skills
- Perform the skill at a sufficient level of difficulty/effort.
  - Not too easy, not too difficult
- Skill should not be performed in isolation, but ideally performed in the context it will be used (strong context-dependence, perhaps also mutual reinforcement).
- Effortful periods should be interleaved with ‘rest’ periods (or engaging in efforts with a different focus; “interval training”).
  - Optimal interval: arguable
- Lengthy practice (e.g., hundreds to thousands of hours)

Optimal Conditions for Learning a Skill

- Must have sufficient motivation
  - Motivation is what seems to ignite the neural circuits that force learning to occur.
    - Evolutionarily (biologically) a number of different "primary" motivators, e.g.:
      - Pain
      - Hunger
      - Fear
      - Procreation
    - "Secondary" motivators (e.g., monetary rewards, long-term goals) are thought by many to ultimately operate through the more phylogenetically ancient mechanisms.
- Motivation is necessary to sustain the intensity and time required.

A.I. Had To Learn Far More Than Motor Skills

Nonverbal Individual with Severe ID



Training of Mental Skills

- There are evolutionary and neurobiologic reasons to believe these are based on much the same mechanisms as perceptual and motor skills.
  - Evolved from same substrate(s)
  - While they appear "innate" in typically developing individuals, may be learnable with proper foundation
- Learning of mental skills seems to have somewhat similar requirements as does learning of motor skills.
  - Deliberate, focused, motivated practice is certainly important (c.f. Kaufman, 2013).

Methods – Conceptual Plan for A.I.

- Educational experience coupled with input from cognitive science/neuropsychology
- Assess skills present at any particular point in time, and determine what is necessary for the next stage.
  - Foundational abilities and prerequisites
    - Attention, choice, rewards (motivations), intent to communicate
  - Basic speech functions
    - Articulation
    - Speech perception
  - Contents of speech/language
    - Words and meanings (e.g., foods, activities)
    - Thought (elements necessary for communication)

Methods – Practical Implementation

- Integrated and coordinated educational and speech program
    - E.g., everyday activities used as opportunities for practicing each skill (e.g., requesting, comprehension, articulation, and vocabulary)
- Varied activities
    - Paced (interval training)
    - Initially, used traditional primary motivators (e.g., mini M&Ms)
    - Later, used tokens, teacher's approval as motivators
- Fostered motivation and communicative intent as well as task performance

Environments for Learning

- A.I. had been taught in one-on-one (teacher) situations.
- Some parallels to what initially happens with typically developing children taught by their parents
- But typically developing humans then begin learning in social situations, e.g.:
  - Sibs
  - Peers
  - Individuals recognized as leaders and authorities

Learning in Social Situations

- It has been argued that social situations are extremely important for humans and other social species.
  - Evolutionary necessity to learn what was important for survival
  - Therefore, all existing perceptual, motivational, and learning mechanisms become very strongly engaged in social situations.
  - There is some evidence that we have evolved distinct mechanisms for learning in social situations → specialized perceptual, conceptual, and motor mechanisms (e.g., facial expressions, speech).
- Currently, social cognition and learning are topics of intense research
  - AZA Stephen Allsop, M.D., Ph.D., Neurology Grand Rounds, Oct. 7: "Understanding Mechanisms and Creating Interventions for Social Cognition and Behavior"

Can Individuals with Autism Benefit from Social Situations?

- Individuals with ASD have “social deficits.”
- Not all of the normal mechanisms for learning in social situations may be impaired in ASD.
- Even if some or all of the mechanisms are impaired, their residual functions may still be powerful enough for them to have a significant role in learning.
  - Particularly if other mechanisms usually responsible for learning are weak or absent
- Speech/language must have evolved from social requirements and are very important for such situations: so mutually reinforcing

Factors in Our Success?

- Many, if not most of the methods used, had been previously described (1970s and in some cases 2500 years before).
- Prior efforts (with A.I. and with other individuals documented in the literature) had used many, if not all, of these methods and materials.
- We believe our methodology had more success for a number of reasons:
  – Selected target skills and methods carefully to be building blocks
    - Coordinated and employed across many situations
    - Data was used to determine efficacy – not wedded to any one methodology or philosophy.
  – Engaged A.I.'s interest, more intense
  – Long-term
  – Eventually, engaged with peers with different types of disabilities

Factors in Our Success?

- Had the resources to do all of this:
  - Financial
  - JHU and SOM connection and background
    - Educational best practices corroborated and refined by cognitive neuroscience perspectives (including outside expertise)
    - Staffing and professional guidance
      - Ability to recruit and retain great teachers (e.g., offer professional career paths; several have gone on to receive PhDs)
    - Research experience
      - Collecting and interpreting data
      - Theoretical notions were subject to empirical tests

Plans

- Use the motivation and experiences that arise with social situations to improve existing skills, and perhaps develop new ones, in these individuals.
  - Set of essentially single-case studies
    - Highly personalized for each individual's motivations, skills, and evolving needs
  - Use the data now increasingly available from audio/video recordings (real-time and offline).

Conclusions and Broader Implications

- May be able to germinate and improve many high-level mental skills and quality of life with the proper approaches.
  - Including skills thought completely out of reach
- Can be clinically valuable for those with severe developmental intellectual disabilities
- Even more might be accomplished with typically developing individuals.
- May be able to identify the most productive behavioral approaches
- When combined with optimal behavioral approaches, neurobiologic methods (e.g., pharmacologic, transcranial direct current stimulation [tDCS] and its variants, transcranial magnetic stimulation [TMS], deep brain stimulation [DBS]) might produce additional improvements

Acknowledgments

- Our deepest thanks to A.I., his parents, his siblings, the other students, and the research subjects who have volunteered over the years.
- Many thanks to John W. Griffin, M.D. (deceased) and Justin C. McArthur, MBBS, MPH, past and current chairs of the Department of Neurology, respectively, and to the JHMI attorneys and administrators, who made the special efforts described here possible. Special thanks to the division's administrators, Nancy Cook (former) and Cristiana Camardella (current).
- The New York Educational Program is privately supported. Major funding for the research component of our activities has been provided by the Therapeutic Cognitive Neuroscience Fund (anonymous donor) with additional funding from the Therapeutic Cognitive Neuroscience Professorship (anonymous donors); the Benjamin and Adith Miller Family Endowment for Aging, Alzheimer's, and Autism; the Department of Defense (DOD #W81XWH-10-1-040); JHU Science of Learning Institute; the National Alliance for Autism Research (NAAR); the NLM Foundation; the Mario Marino Fidelity Charitable Gift Fund; Maharba Inc.; Frimex Investment LLC; the Binder Family Charitable Fund; the Murren Family Foundation; the Wockenfuss Endowment and Fund; and the Bernard Gordon Memorial Fund.

Acknowledgments

- Special thanks to the directors of the New York Educational Program: Jessica O'Grady, founding director and current research director; Jennifer (Juska) Carolan; Jennifer Thorne; and Olivia Pullara (current director). Special thanks to all the associated teachers, speech pathologists, art teachers, personal trainers, music teachers, and others based in New York and involved in these efforts to date, including, but not necessarily limited to, the following (in alphabetical order): Melissa Allen, Brenda Armour, Brian Bacchi, Yodit Berhanou, Christina Birkhead, Johnny Bontemps, Anthony Canty, Emily Carangelo, Eric Chessen, Lisa Marie Darling, Dr. Katie Davis, Anne Fetherston, Zachary Fisher, Jeseraire Francis, Eric Frantino, Damaris Frias, Jackeline Giansanti, Baris Goturk, Liam Gooley, Allison Gordon, Dr. Jordan Grafman (Northwestern U.), James Hesky, Judy Horne, Matt Kaplowitz, Robert Kieger, Kathleen Keller, Sandra Kennedy, Amanda Kessler, Natasha Ilyne King, Dr. Kara Kulba, Erin Loughlin, Sydney Magliola, Emilie Mankopf, Lauren Moskowitz, Aaron Mattfeld, Megan Miller, Adam Pakiela, Penelope Ream, Chayim Rosensweig, Angela Ruggiero, Wendy Sapp, Lucy Schlosser, Lindsay Sheldon, Ann Shirley, Erin Staub, Steven Troyer, Alethea Vasilas, Rebecca Vitagliano, Christy Yoon

Acknowledgments

- Special thanks to the Baltimore-based individuals involved in these efforts to date including, but not necessarily limited to, the following (in alphabetical order): Dr. Dana Boatman, Maureen Boner, Dr. Katarina Boser, Laura Bosley, Dr. Xiaoqian Chai, Mariya Chernenok, Dr. Emily Coderre, Alessandra Dallavecchia, Dr. Joseph Dien, Robert Glatzer, Hanna Glazer, Amy Greiser, Nancy Grund, Julia Hernandez, Dr. Sharon Kuo, Ross Lawrence, Dr. Kerry LeDoux, James Livengood, Dr. Nazbanou (Bonnie) Nozari, Pat Ourand, LaQuata Pascarell, Erin (Andersson) Pickett, Dr. Brenda Rapp (JHU), Dr. Sarah Reusing, Dr. Rosalind J. Sadleir (U of Fl), Dr. David Schretlen, Jennifer Shea, Dr. Richard Skolasky, Dr. Craig Stark (JHU), Shauna Stark, Monica Sullivan, Dr. Kyongje Sung, Dr. Joseph van Steenburgh, Dr. Tracy Vannorsdall, Mark Varvaris, Johanna Veader, and Dr. Jacqueline Weaver.

- These efforts benefited from consultations, conversations, and comments by many other individuals, including the teachers and speech pathologists at A.I.'s school; the parents and caregivers of the other individuals enrolled in our educational and research programs; Drs. Rebecca Landa and Andrew Zimmerman (KKI); Dr. Ruth Nass (NYU), Dr. Ivaar Lovaas (UCLA, deceased); Drs. Liz Bates (UCSD, deceased); Dr. Derek Bickertom (U Hawaii), Dr. Vicky Fromkin (UCLA, deceased); Dr. Lynne Bernstein (House Ear Institute); Dr. Diana Van Lancker (NYU); Dr. Mariale Hardiman (JHU); Dr. Barbara Landau and others with the JHU Science of Learning Institute; Drs. Michael McLoughlin, Grace Hwang, Phillippe Burlina, Konstantinos Gerasopoulos, Ariel Greenberg, Bart Paulhamus, Michael Wolmetz, Mr. Cash Costello, and others at JHU's Applied Physics Lab; Drs. Omar Ahmad and Steven Zeiler (JHMI); and many others.

Acknowledgments

- Very special thanks to my youngest son, my spouse, and my oldest son, for their inspiration and very special contributions, and to the clinicians, educators, speech pathologists, and others who have been involved in my youngest son's care for their insights and efforts.
- Robert Glatzer, Nancy Grund, Jessica O'Grady, and Tim Phelps (from the SOM Art Graduate Program) were particularly involved in the preparation of this presentation. But any errors, omissions, misstatements, or muddling are my responsibility.
- For a current list of faculty, associated faculty, and staff, see http://web.jhu.edu/cognitiveneurology
- Slides from this talk (redacted) and selected references are at http://web.jhu.edu/cognitiveneurology

Video source

- Slide 22: Max Planck Institute: Echtzeit-MRT-Film: Sprechen https://www.youtube.com/watch?v=6dAEE7FYQfc

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Thank You! Any Questions?