Alternatives to Medication

- ★ Supplements: One or Two You May Not Have Heard Of
- ★ Neurofeedback Revisited
- ★ TMS in Adolescents
- ★ The Light Box
- ★ Cogmed Working Memory Training
- ★ Interactive Metronome

David Mitnick . Bruce Friedman
Nicole Garcia . Laurie Kalb

Supplements: One or Two You May Not Have Heard Of

Old Bugs, an Orphan Drug and a Shameless Plug:

3 Quick Takes on Autism Spectrum Treatments:

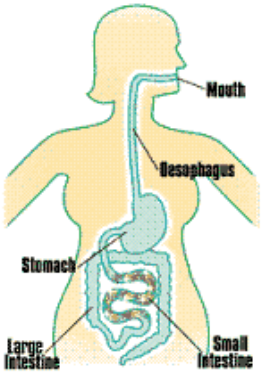
Probiotics

Respen-A

QEEG-Guided Neurofeedback

Probiotics- a teaser

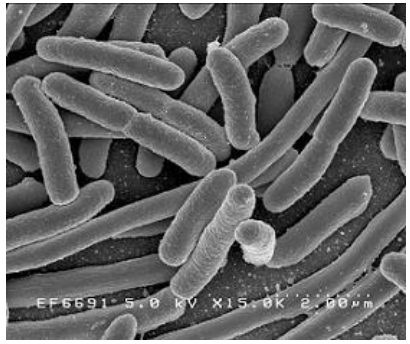
Good guys in the gut



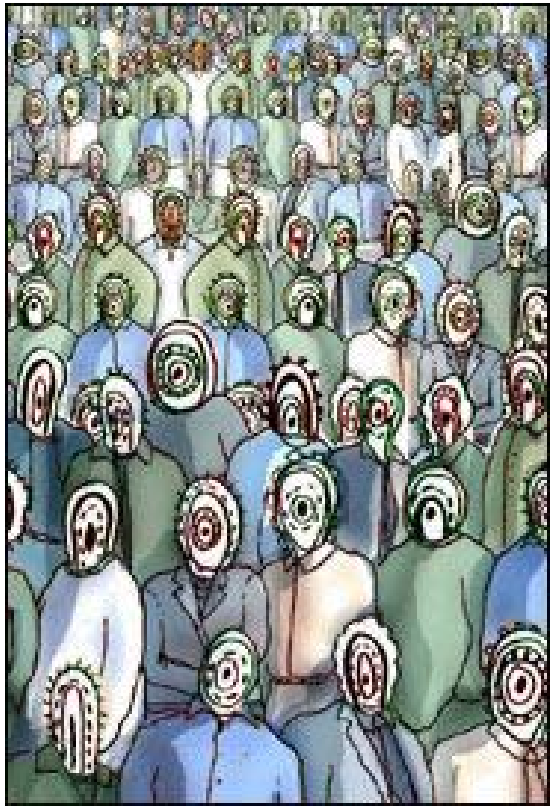
- GI tract is **sterile** until birth
- **Colonization** begins immediately after birth and is nearly complete by one week of life, but quantity and species vary markedly over the first 6 months of life and is “adult” by 2 yrs
- More than **1000 species** have been found, each with numerous strains
- Easier to detect via molecular means than by culture

Microbes in the gut – our Flora

- Neonatal, childhood, and adult flora differ based upon environmental factors :
  - Mode of delivery (C/S vs vaginal)
  - Hygiene measures
  - Maternal flora
  - Breast vs formula feeding
  - Antibiotic exposure
  - Diet



Fun facts about flora

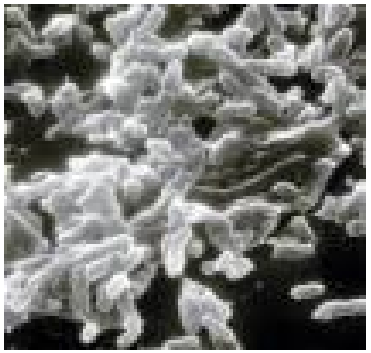


- **We have 10^{12} viable bacteria/gm of large bowel content which is more bacteria in one person's gut than there have ever been humans on the planet - 10 trillion bacteria which weigh ~ 3 lbs**
- **There are 10 X more bacteria in the gastrointestinal lumen than the number of cells in the human body**
- **There are 100 X the human genome's DNA content in those bacteria**
- **The metabolic activity of the intestinal flora is greater than that of the liver's**

“Bugs” aren’t always bad

- Intestinal bacterial flora are there for a reason
- Interact with the immune system of the host
- Compete with pathogens for space and resources in the intestines
- We get short chain fatty acids (Vit K etc) for our metabolic pathways
- Humans get heat from the metabolism of indigestible (to us) compounds

Old friends



- Mammalian evolution has kept us in close contact with relatively harmless micro-organisms over a long period of time
- We recognize these “old friends” and they help to educate our immune system
- Decreased types of bacteria in our gut from antibiotics similar to effect of global warming to the planet

Probiotics

- **Probiotic bacteria can modulate abnormal gastrointestinal immune responses:**
  - **Suppress either antibody-mediated or T cell mediated hypersensitivity to food so decreases gut inflammation**
  - **Increases secretory IgA production**
  - **Decreases gut permeability**
  - **Stimulates NK cells**
  - **Increases IL-10 production so improves immune regulatory function**

Fermented Foods – Rich in Probiotics

Functions of good bacteria

- Regulate peristalsis and bowel movements
- Break down bacterial toxins
- Make vitamins needed and utilize: B1, B2, B3, B5, B6, B12, A and K
- Digest protein into amino acids (for use by the body)
- Produce antibiotics and antifungals
- Help breakdown sugars, lactose, and oxalates
- Support immune system and increase number of immune cells
- Balance intestinal pH
- Protect against environmental toxins: mercury, pesticides, pollution

Raw fermented foods contain billions of bacteria/serving!

Gastrointestinal microflora studies in late onset autism

- Some cases of late-onset (regressive) autism may involve abnormal flora because oral vancomycin, which is poorly absorbed, may lead to significant improvement in these children.

- Fecal flora of children with regressive autism was compared with that of control children, and clostridial counts were higher.

- The number of clostridial species found in the stools of children with autism was greater than in the stools of control children.

- Children with autism had 9 species of Clostridium not found in controls, whereas controls yielded only 3 species not found in children with autism.

- In gastric and duodenal specimens, the most striking finding was total absence of non-spore-forming anaerobes and microaerophilic bacteria from control children and significant numbers of such bacteria from children with autism.

Finegold et al., 2002 Clin Infect Dis 35(Suppl 1):S6-S16

A double-blind, placebo-controlled probiotic feeding study in children diagnosed with autistic spectrum disorders

- The potential of Lactobacillus plantarum WCSF1 (a probiotic) to modulate the gut microbiota of autistic subjects was investigated during a double-blind, placebo-controlled, crossover-designed feeding study.

- The faecal microbiota, gut function and behaviour scores of subjects were examined throughout the 12-week study.

- Lactobacillus plantarum WCFS1 feeding significantly increased Lab158 counts (lactobacilli and enterococci group) and significantly reduced Erec482 counts (Clostridium cluster XIVa) compared to placebo.

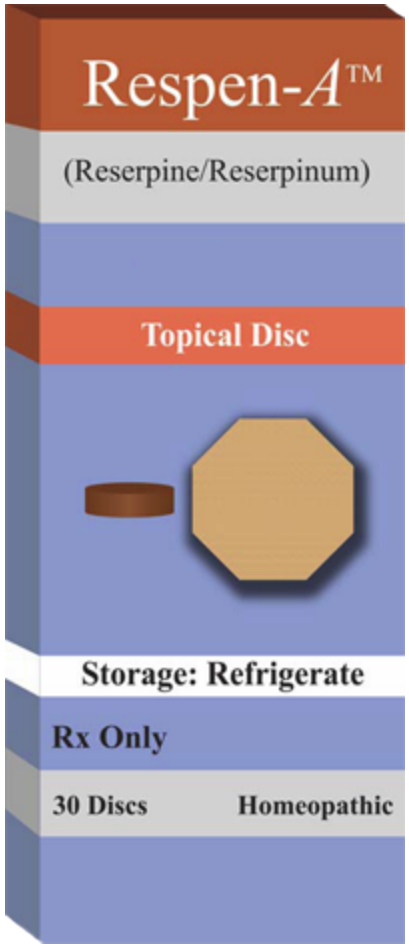
- Probiotic feeding also resulted in significant differences in the stool consistency compared to placebo and behaviour scores (total score and scores for some subscales) compared to baseline.

Parracho, et al., 2010 International Journal of Probiotics and Prebiotics 5(2):69-74

Clostridia: Potential Treatments

Probiotics (Consider higher potency and broad spectrum)

- Lactobacillus acidophilus
- Saccharomyces boulardii
- Lactobacillus rhamnosus GG
- Lactobacillus plantarum
- Bifidobacterium breve
- Bifidobacterium longum
- Bifidobacterium infantis
- Lactobacillus paracasei
- Lactobacillus bulgaricus
- Streptococcus thermophilus



Respen-A™

Homeopathic Treatment

For Symptoms Of

Impaired Social Interaction, Impaired Communication and Repetitive Behaviors.

Developed and Patent Pending

by

Neuro-Med

(Homeopathic Division of MedDEV Inc)

If you want a more detailed description of a slide you are viewing, simply click on the speaker icon shown on the slide. Press F5 to begin slide show. Click mouse or hit space bar to advance to next.

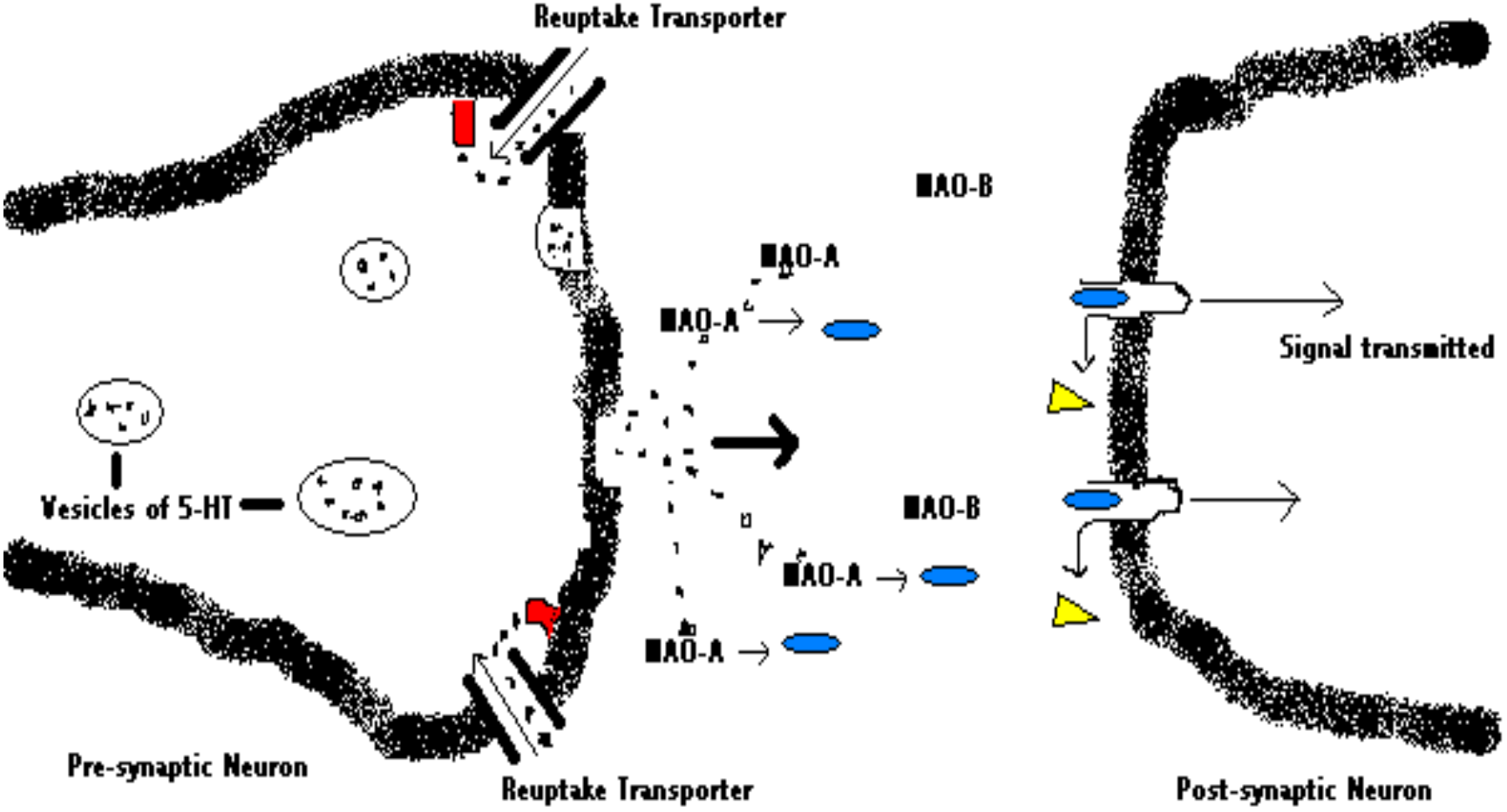
Hypothesis:

Decreased MAO-A activity can result in Autism

Monoamine Oxidase-A (MAO-A)

- MAO-A is a mitochondria enzyme in the brain and liver
- Metabolizes serotonin, norepinephrine and histamine into the active aldehyde metabolites

Metabolism of Serotonin (5-HT) Into the Active Metabolite 5-HIAL



5-HT (Serotonin)

5-HT1A receptor When activated inhibits serotonin release and inhibits MAO-A activity

5-HIAL Active Metabolite on Post-synaptic receptor —(Active aldehyde)

5-HIAA Excreted Metabolite

Factors That Decrease MAO-A Activity

- Genetic– expressed on the X chromosome
  - High and low activity alleles
- High estrogen levels
- Aluminum, mercury, high copper and cadmium levels
- Stress
- Lipid peroxidation from the breakdown of polyunsaturated fats

MAO-A Deficiency

- Can result in abnormal behavior and mental retardation
- Results in elevated levels of serotonin and norepinephrine and histamine.
  - May cause impairment in fine and gross motor movement
  - Increase in allergies and food sensitivities

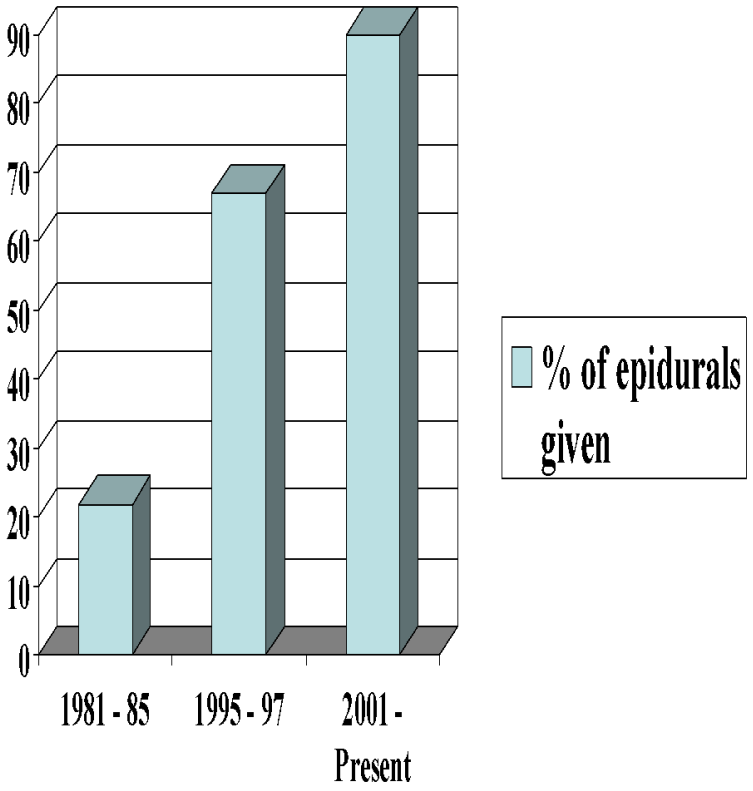
High Serotonin Levels

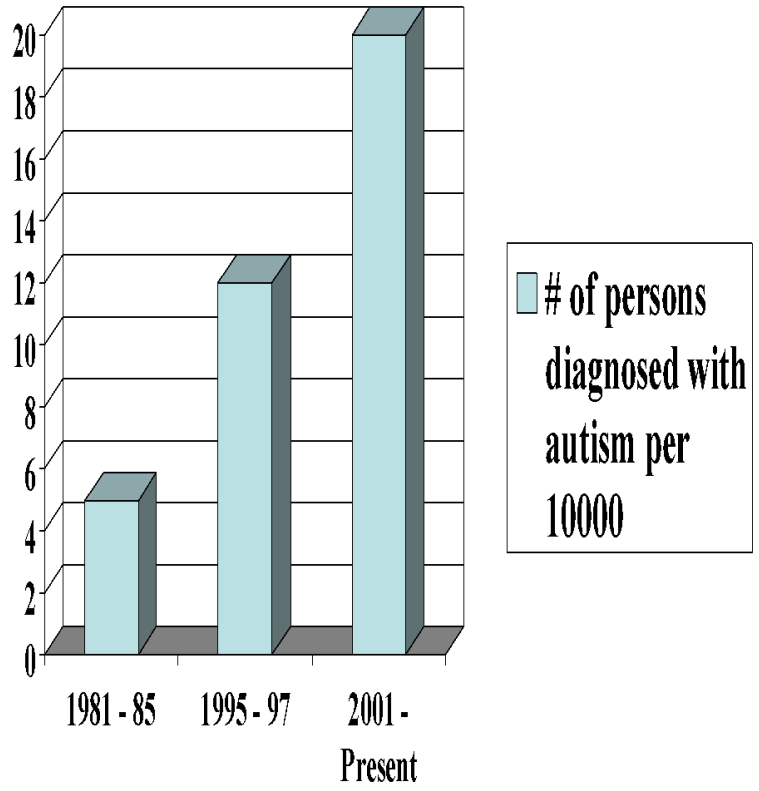
- Stimulate the release of ACTH
- Stimulate the release of proopiomelanicortin hormone
  - Results in increased Beta-endorphin production
- Inhibits the growth of oxytocin neurons
  - Needed for social and communication skills, language development, bonding

Possible Contributing Relationships to the Development of Autism

- Genetic transfer of low activity allele
  - Maternal depression and personality disorders increase the risk of autism in offspring
  - Males have increased genetic risk
- Epidural with Pitocin (synthetic oxytocin) augmentation
  - Bupivacaine, Ropivacaine, and Pitocin share the same cytochrome P450 pathway cyp3A4
  - Ropivacaine (1996) requires more to be used competing more for the cyp3A4
  - Ropivacaine also can cause serotonin syndrome with SSRI so may inhibit MAO-A
  - Females have more cyp3A4
  - Neonatal oxytocin manipulation inhibits AVP receptor binding and this would effect boys more than girls
- Mercury and aluminum in vaccines inhibit MAO-A and mercury inhibits oxytocin
- MAO-A decreases with age so may explain why autism is often diagnosed after 3 years of age

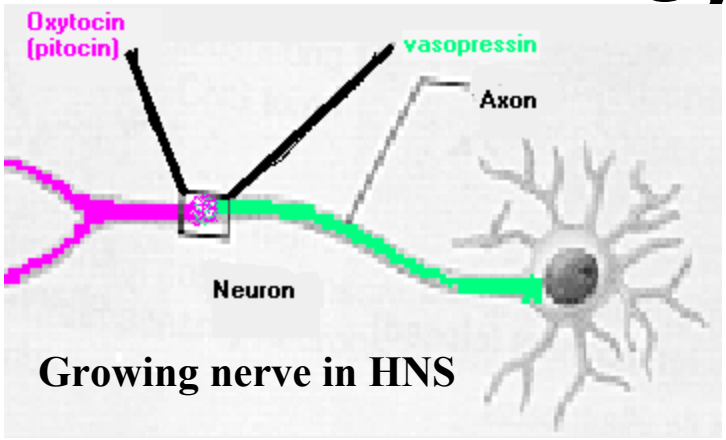
Percentages of Epidurals vs. Number of Autism Cases





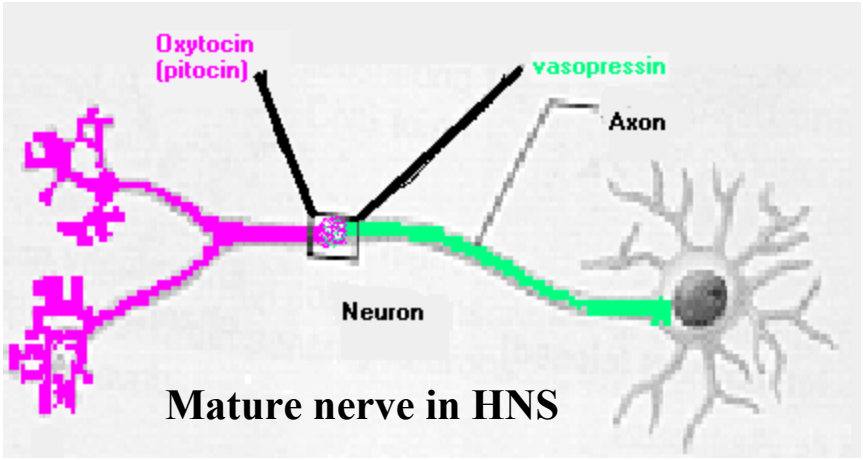
http://www.hhs.gov/factsheets/fs_tableVII_doc.2.htm

Oxytocin Mediates the Growth of the Hypothalamus –Neurohypophysial System



Growing nerve in HNS

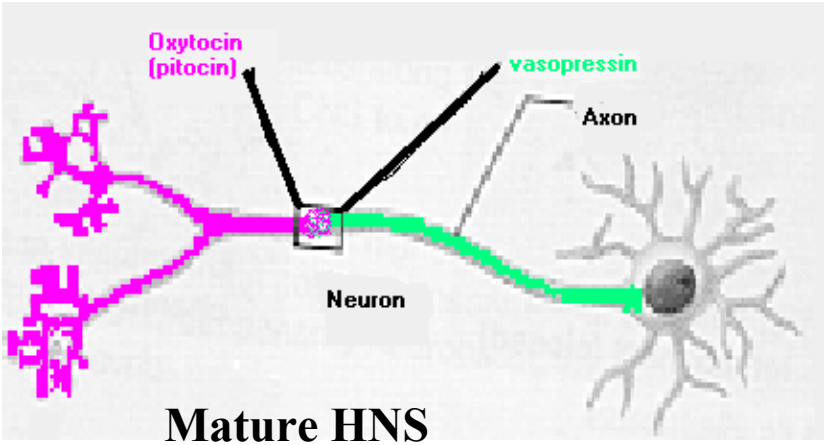
This nerve system is called the Hypothalamus-neurohypophysial-system (HNS) and is involved in the limbic (emotional) and social behaviors.



Mature nerve in HNS

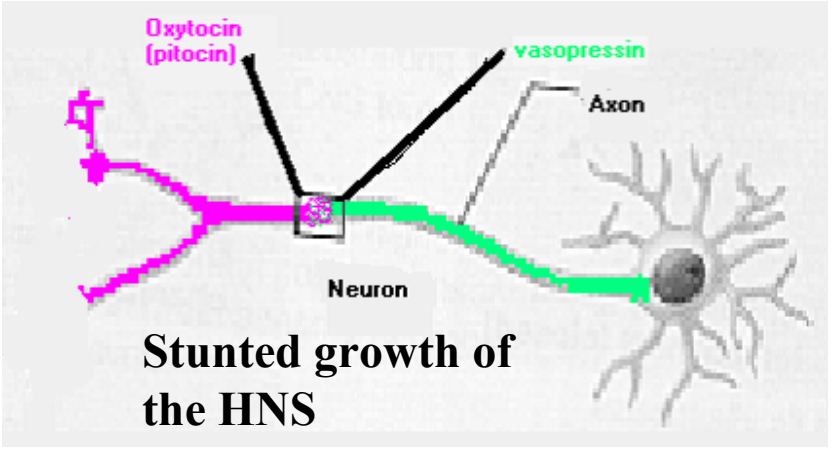
Vasopressin changes to Oxytocin as the nerve grows. When Oxytocin reaches a certain level, it tells the nerve to quit growing. This is supposed to reach this level 7-10 days postpartum.

High Level of Pitocin (oxytocin) During Childbirth May Result in Stunted Growth of HNS



Mature HNS

- Often increased doses of Pitocin are required when a woman has an epidural during childbirth augment the contractions because the woman may not push effectively with an epidural.



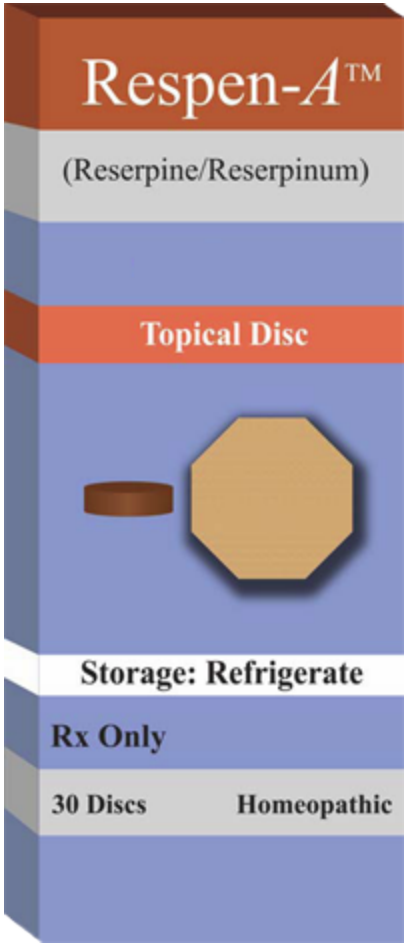
Stunted growth of the HNS

- This may result in the oxytocin level getting high enough to signal the HNS to stop growing in the baby as seen in the bottom diagram.

Hypothetical Scenario

- Mother has a low activity allele that gets passed on to offspring (son at most risk).
  - If mother has depression, high copper, cadmium, aluminum or mercury, lipid peroxidation, stress, high estrogen could result in elevated serotonin level exposure to fetus and this can inhibit oxytocin neuron growth
- Mother is given epidural and pitocin (synthetic oxytocin) during childbirth
  - This may trigger the neurohypophysial system to quit growing
  - Results in decreased oxytocin production and AVP receptor binding
- Infant may be born with inadequate neurohypophysial system, decreased AVP receptor binding and low activity MAO-A so serotonin and norepinephrine levels elevate
  - As child ages the MAO-A activity becomes inadequate and serotonin and norepinephrine levels elevate more
  - High serotonin levels inhibit oxytocin neuron growth further.
- Children at a very young age are given vaccinations containing mercury and aluminum
  - Which inhibit oxytocin and MAO-A
- Child is diagnosed with Autism

So What Does This Have to Do With Respen-A?



- Respen-A contains reserpine (reserpinum) that has been shown in research to increase the activity of MAO-A
- This may decrease the levels of serotonin and help reduce symptoms of impaired social interaction, impaired communication and repetitive behaviors.

Neurofeedback Revisited

Neurofeedback teaser

QEEG-Guided Neurofeedback Approach

for

Autism Spectrum Disorders:

Focus on Mirror Neuron Dysfunction

The Problem

Many individuals with autism spectrum traits exhibit evidence of mirror neuron dysfunction

- Altered expression of empathy
- Diminished capacity to infer another's intentions
- Motor coordination problems
- Diminished reading of social situations and facial expressions

Mirror Neurons

- Mirror neurons represent a distinctive class of neurons that discharge both when the individual executes a motor act and when it observes another individual performing the same or a similar motor act. These neurons do not discharge in response to the simple presentation objects. They also do not discharge, when the individual observes motor actions mimicked without the target object.

Role of Mirror Neurons

- There are two distinct series of information that one can get observing an action done by another individual. One is "what" the actor is doing; the other is "why" the actor is doing it. If we see, for example, a girl grasping an apple, we understand that she is grasping an object. Often, we can also understand, in addition, why she is doing it, that is we can understand her intention. We can infer if she is grasping the apple for eating it, or for putting it into a basket.

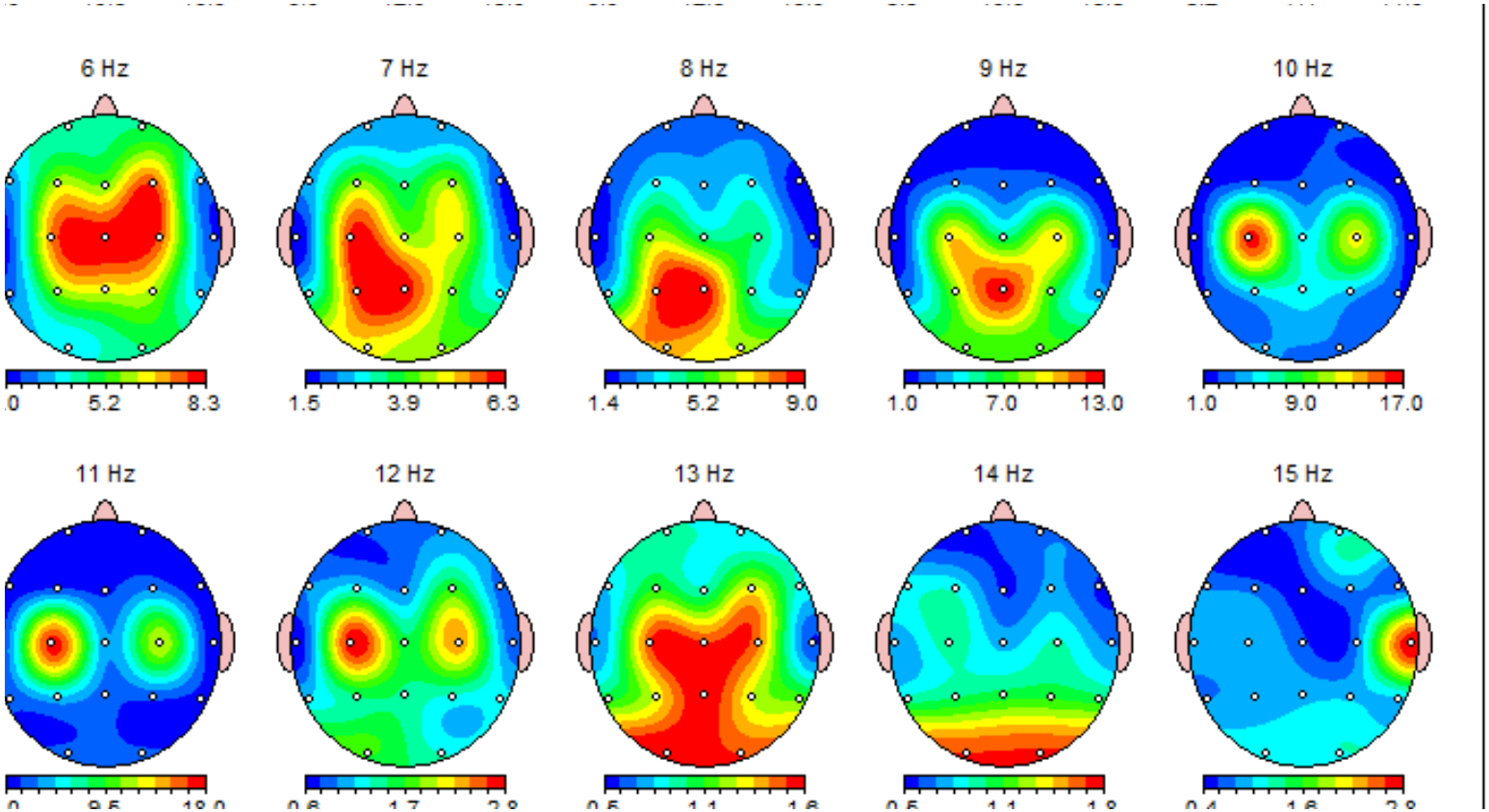
Role of Mirror Neurons

- Although the hypothesis that mirror neurons are involved in intention understanding has been proposed several years ago (Gallese and Goldman 1998), only recently, however, this hypothesis has been supported by an fMRIexperiment.
- In this experiment volunteers were presented with hand actions without a context and hand actions executed in contexts that allowed them to understand the intention of the action agent.
- The main result of the study was the demonstration that **actions embedded in contexts yielded selective activation of the mirror neuron system**.
- This indicates that mirror neurons, in addition to action understanding, also **mediate the understanding of others' intention** (Iacoboni et al. 2005).

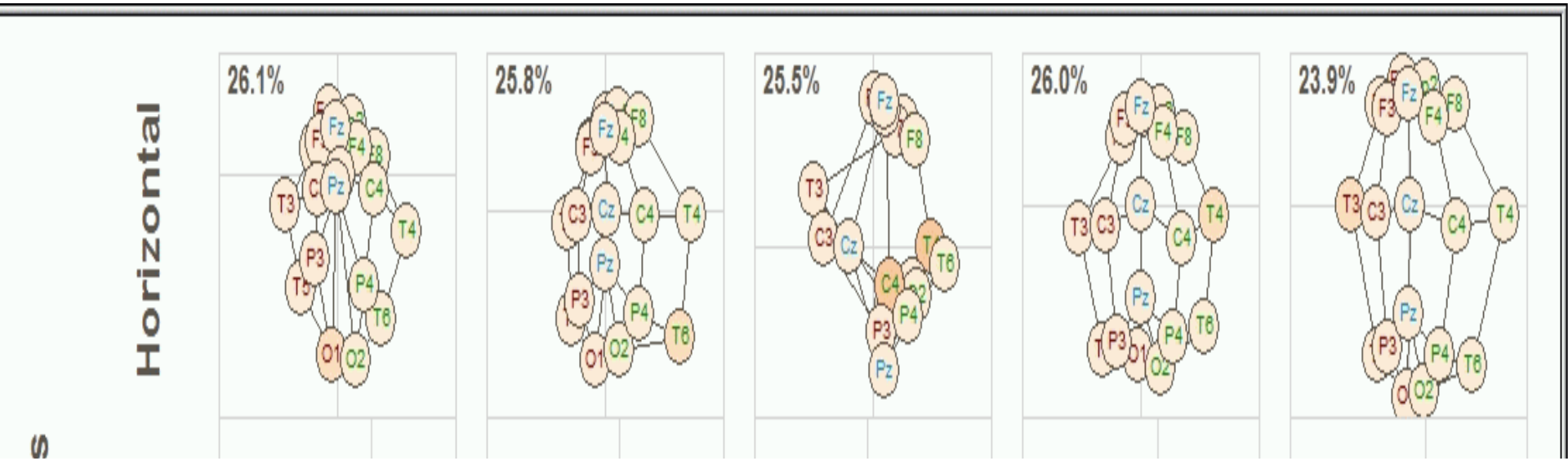
Mu Rhythms

- (EEG) or brain wave patterns which have a frequency of 8-13 hertz, or oscillations per second
- mu rhythms typically are suppressed by mirror activity in premotor areas of the brain
- this does not happen in children with autism (generally)

Mu Rhythm on QEEG



Mu Rhythm on QEEG



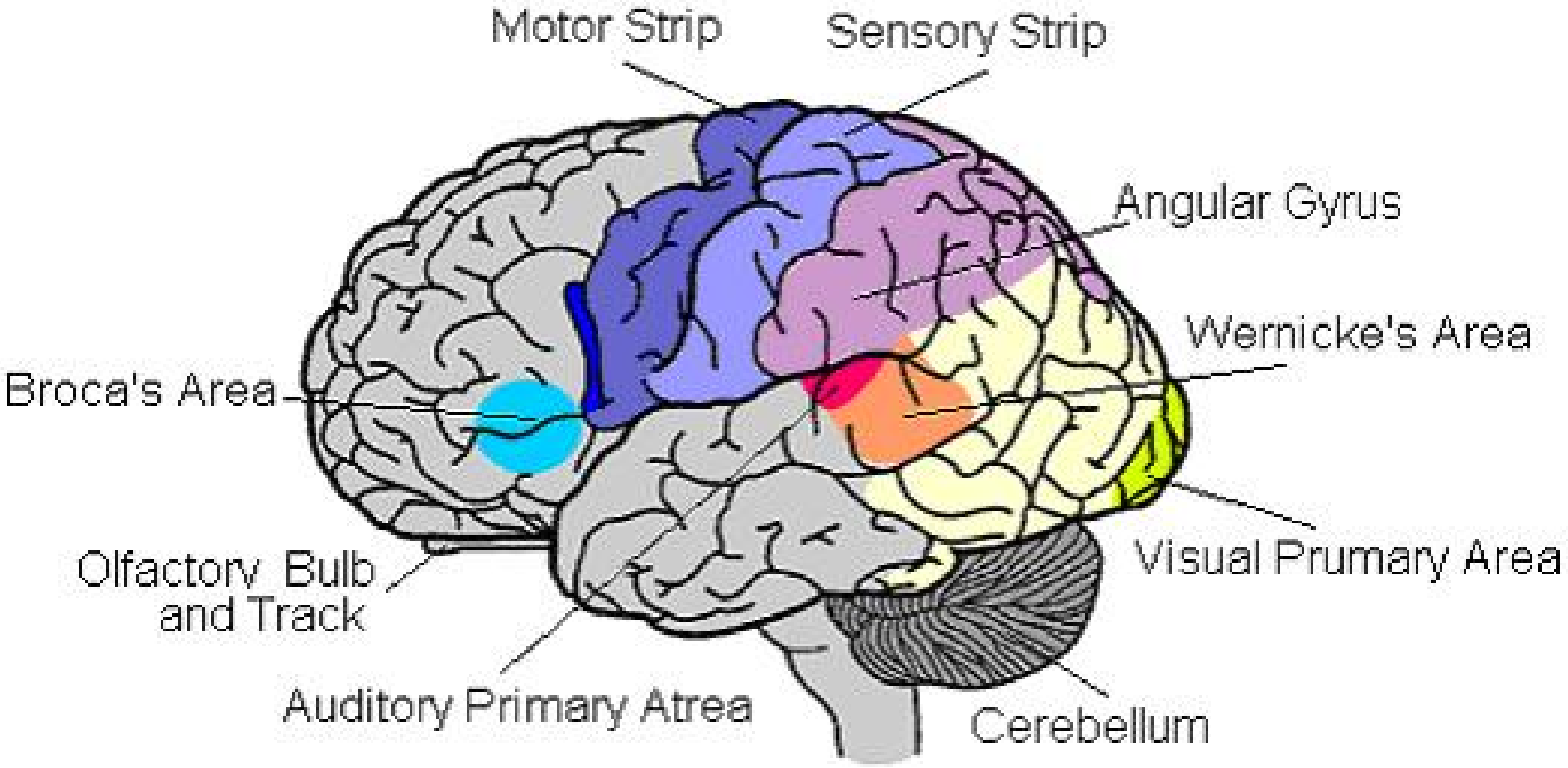
QEEG-Guided Neurofeedback

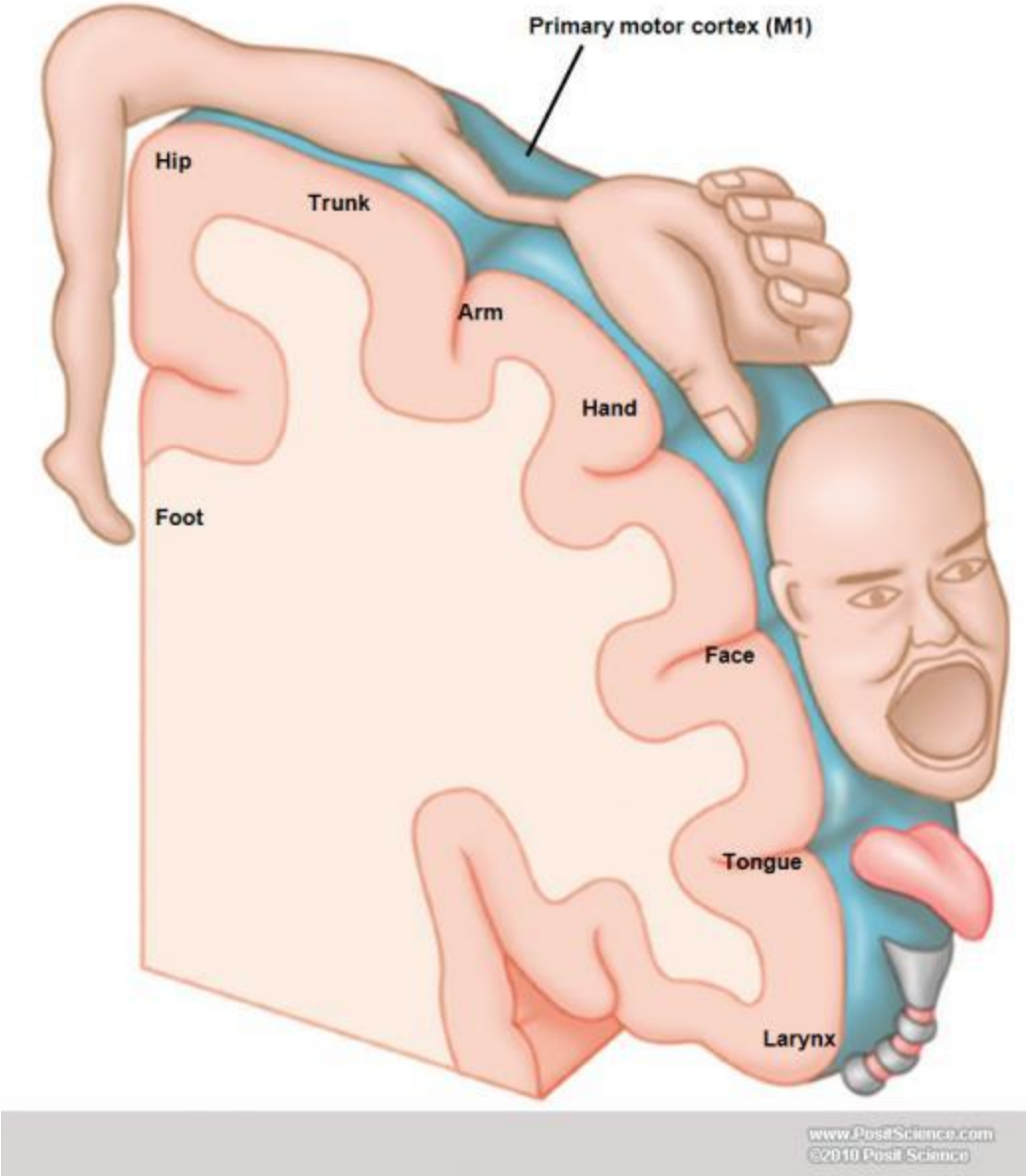
- We have magnitude, location and frequency information about the mu rhythm
- Patient (brain) is rewarded in terms of the feedback when parameters set for approximating the goals from the databases in the QEEG are met
- Repetition of the exercise over weeks to months to consolidate a new patterns that shows increased activation of the mirror neuron system and suppression (desired) of the mu rhythm
- Correlates with improvements in behaviors associated with mirror neuron functioning

Results when successful

- Improved reading of facial expressions
- Improved eye contact and socially relevant attention
- Improved imitation (motor and social)
- Improved understanding of social situations, empathic expression and inference regarding others' intentions and feelings

TMS in Adolescents


Motor Strip
Sensory Strip
Angular Gyrus
Wernicke's Area
Broca's Area
Olfactory Bulb
and Track
Visual Prumary Area
Auditory Primary Atrea
Cerebellum


Primary motor cortex (M1)
Hip
Trunk
Arm
Hand
Foot
Face
Tongue
Larynx
www.PostScience.com
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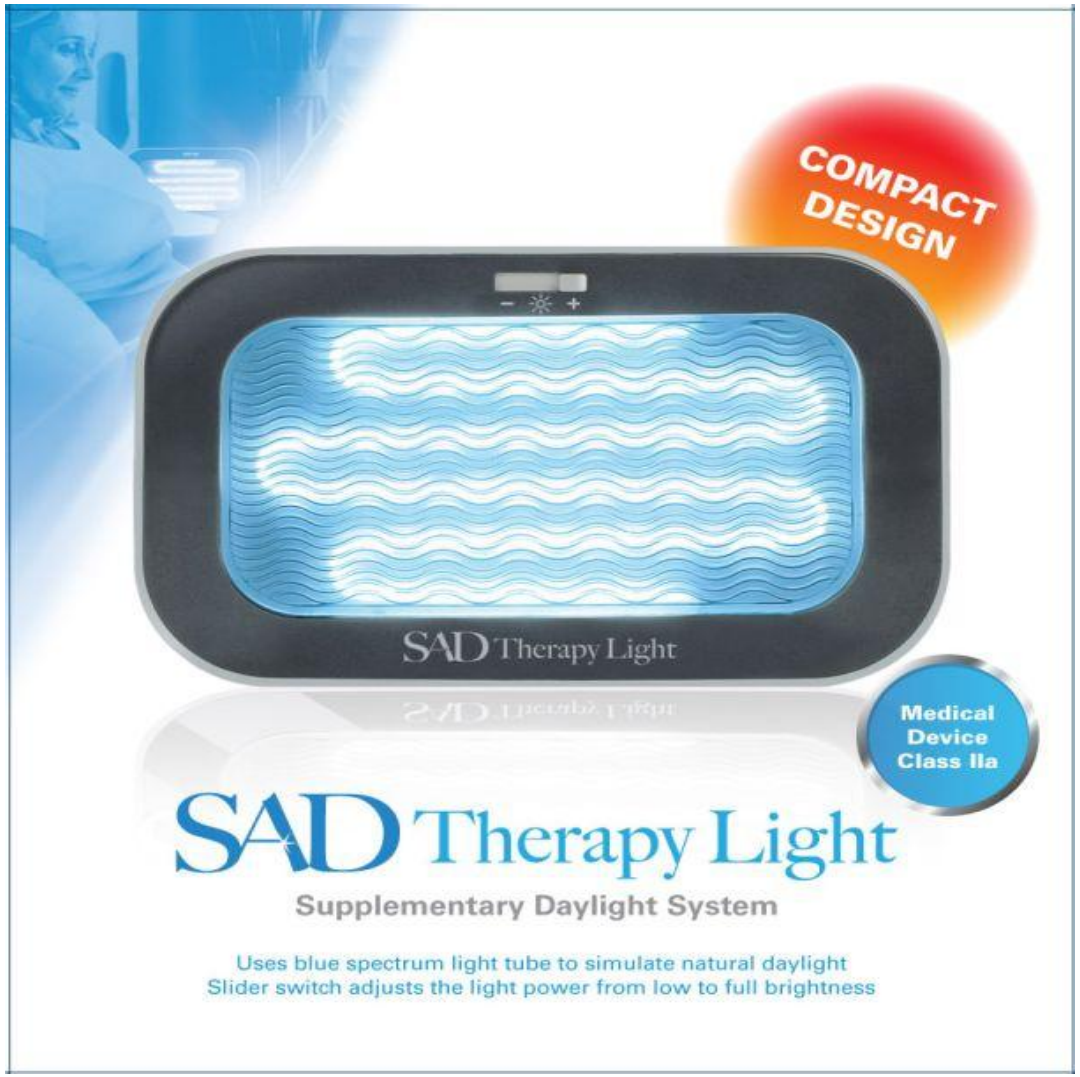
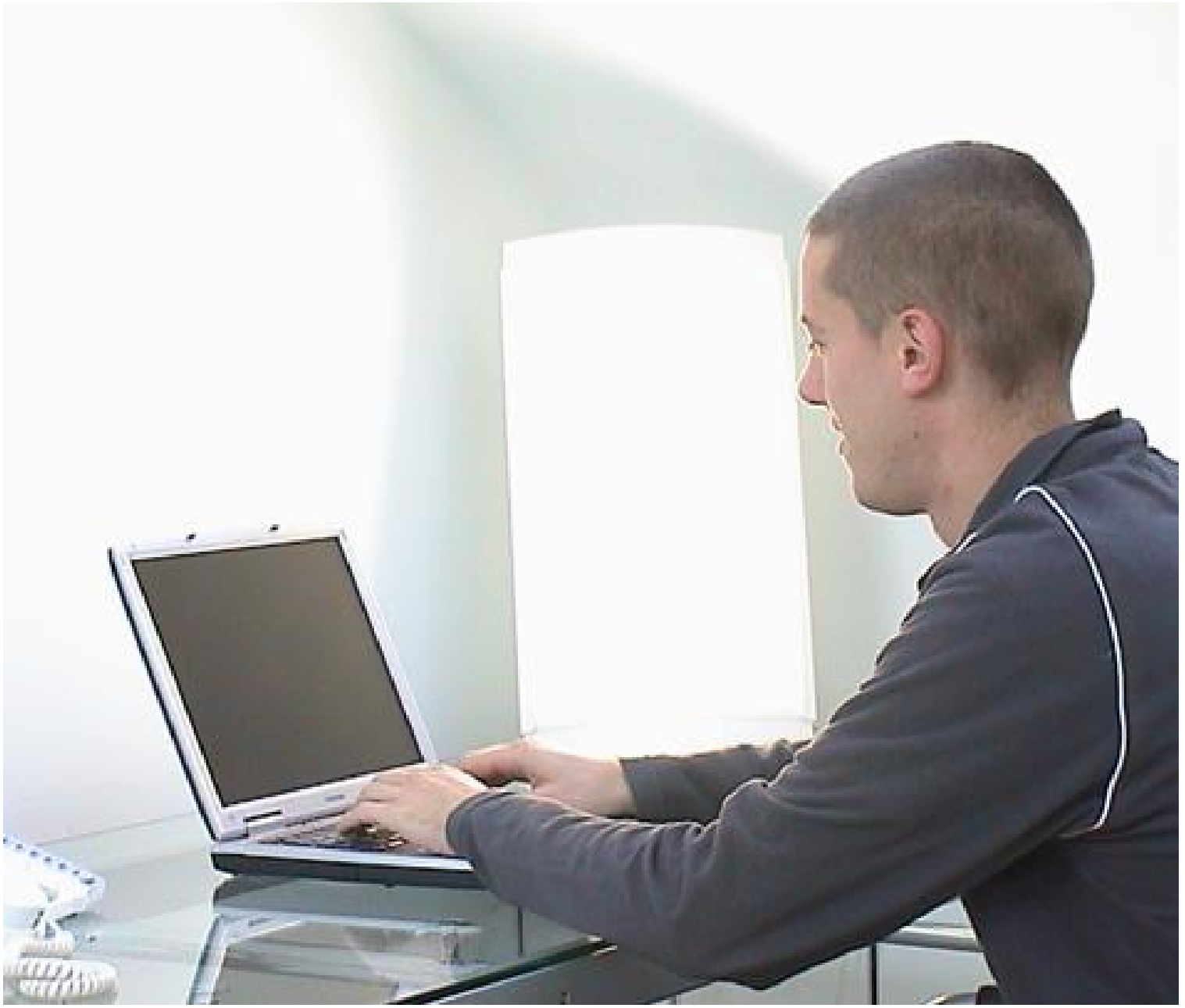
The Light Box



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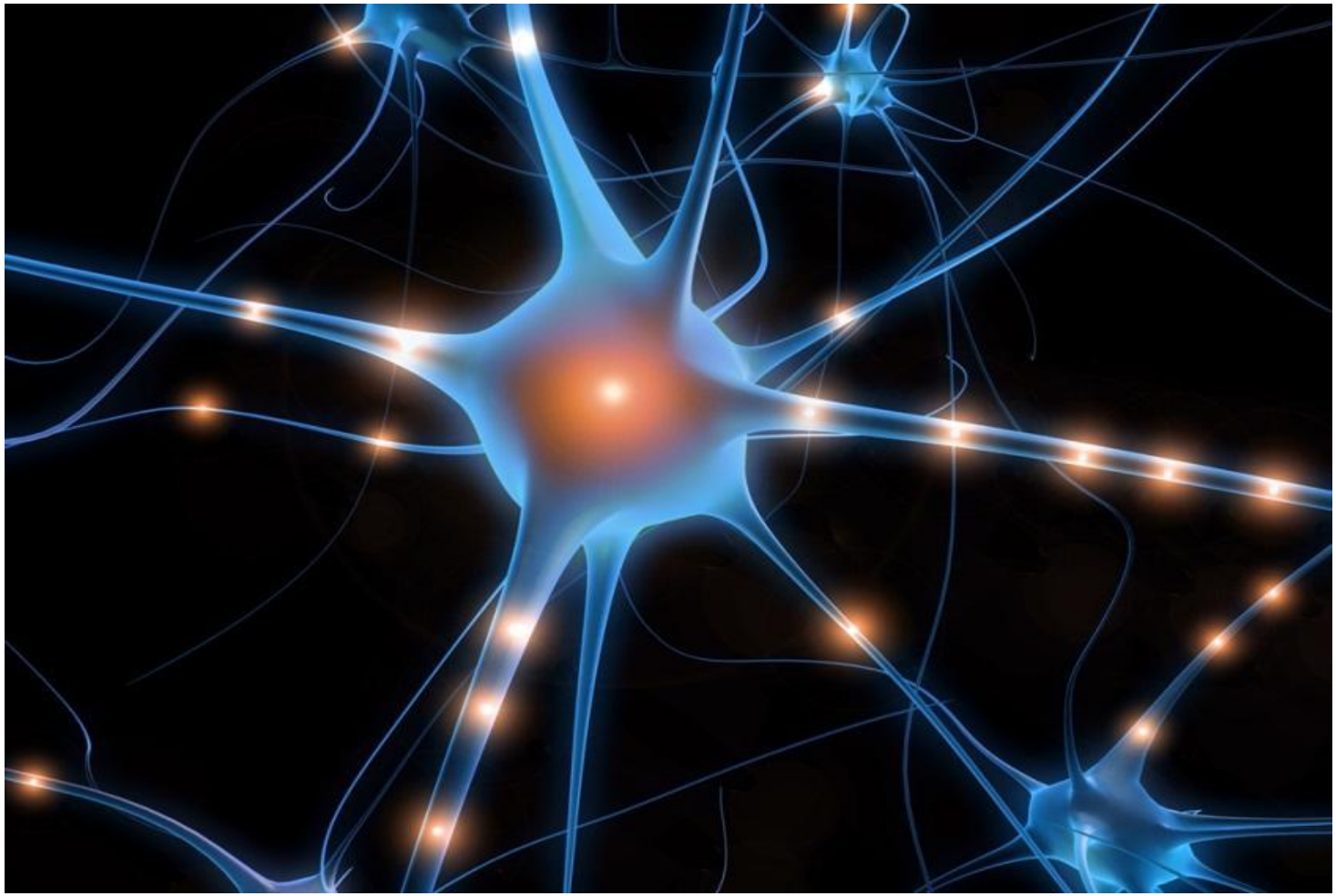
Cogmed Working Memory Training



What is Working Memory?

The ability to keep information in your mind for a short period of time (seconds) and be able to use the information in your thinking

- ✓ Prefrontal & parietal cortex, basal ganglia & dopaminergic transmission
- ✓ Central to concentration, problem solving, impulse control & most executive functions
- ✓ Closely correlated to fluid intelligence & strong indicator of academic & professional success

Why Does Working Memory Matter?

- ✓ **Academic Functioning:** reading comprehension, math calculation, word problems, drawing inferences in writing
- ✓ **Emotional Regulation**: frustration tolerance, delaying gratification
- ✓ **Social Functioning**: solving problems with peers & family
- ✓ **Executive Functioning**: following instructions, organizing, planning ahead, following through
- ✓ **Recreational Functioning**: organized, structured team activity

Working Memory & Academic Performance

- ✓ **10-15%** of all students have WM deficits
- ✓ Below average performance in most areas of learning
- ✓ Learning disabilities & ADHD
- ✓ Standardized tests results driven by WM
- ✓ School success predicted better by WM than IQ
- ✓ WM is crucial for academics & school-related tasks

Makes WM Training Possible

- ✓ The brain can physically change in response to **focused repeated intensive activity/training**
- ✓ Improved working memory **generalizes** to other cognitive abilities and behavior
- ✓ Effects are strong and lasting
- ✓ Klingberg (2002)

What is Cogmed Working Memory Training?

1. **Scientific** – designed by leading neuroscientists
2. **Adaptive** - in real time
3. **Intensive** – hard work
4. **Sustained** – 25 sessions
5. **Supported** – your coach will be there
6. **Targeted** – WM only

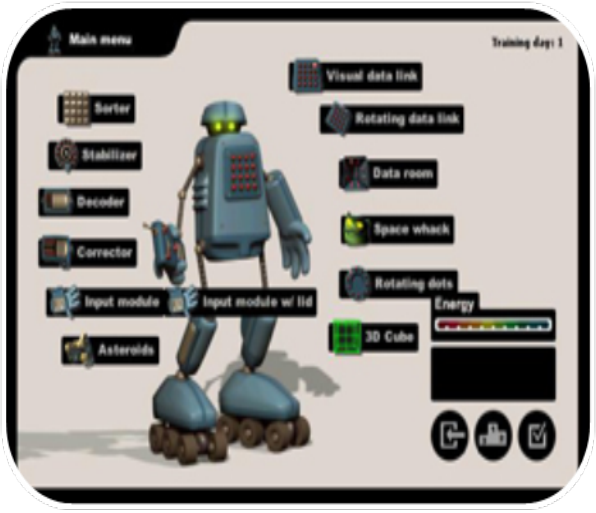
Who is Cogmed Training for?

- Identified working memory deficits
- Inborn: learning disabilities, attention problems
- Sudden: TBI, stroke
- Gradual
- Increased demand
- Complementary to other interventions
- Contraindications

3 Versions of Cogmed

Cogmed JM

Pre-school (4-6)



Cogmed RM

Child/Adolescent (7-17)

(~75% of all clients, including adults)

Cogmed QM

Adult (18-up)

Cogmed: Start to Finish

Structured Consultation → Start-up session → 25 training sessions (8/12 exercises) & weekly coach calls → 1-Month Wrap-up & extension training → 6-Month Follow-up & extension training plus

Key Research Findings to Date

- ✓ **80%** see training effects after 1 month
- ✓ Increased effects seen after 6 months
- ✓ Improvement can be tracked by on **three levels**:
  - fMRI/PET (increased brain activity in pre-frontal and parietal lobes; increased dopamine D1 receptors)
  - neuropsychological testing
  - rating scales
- ✓ Improved WM **generalizes** to behavioral improvement
- ✓ Behavioral improvement is **sustained** over time

Key Changes Observed

Clients say that they:

- can concentrate better in class/at work
- perform better on exams
- remember better, generally and/or specifically
- cannot forget things as easily
- are less restless

Teachers say the student:

- is calmer
- concentrates more/sustains attention for longer periods of time
- performs better on academic tasks
- shows greater interest in school work

Key Changes Observed

Parents say their child:

- communicates better
- is more focused
- Shows more initiative in chores & tasks (e.g. homework)
- is more organized
- Is neater in their room & their grooming
- remembers directions & routines better
- has better frustration tolerance & fewer meltdowns
- has improved social interaction
- has improved test performance
- has greater self-confidence

Cogmed Demonstration

Cogmed Training Web

Interactive Metronome


thank you!