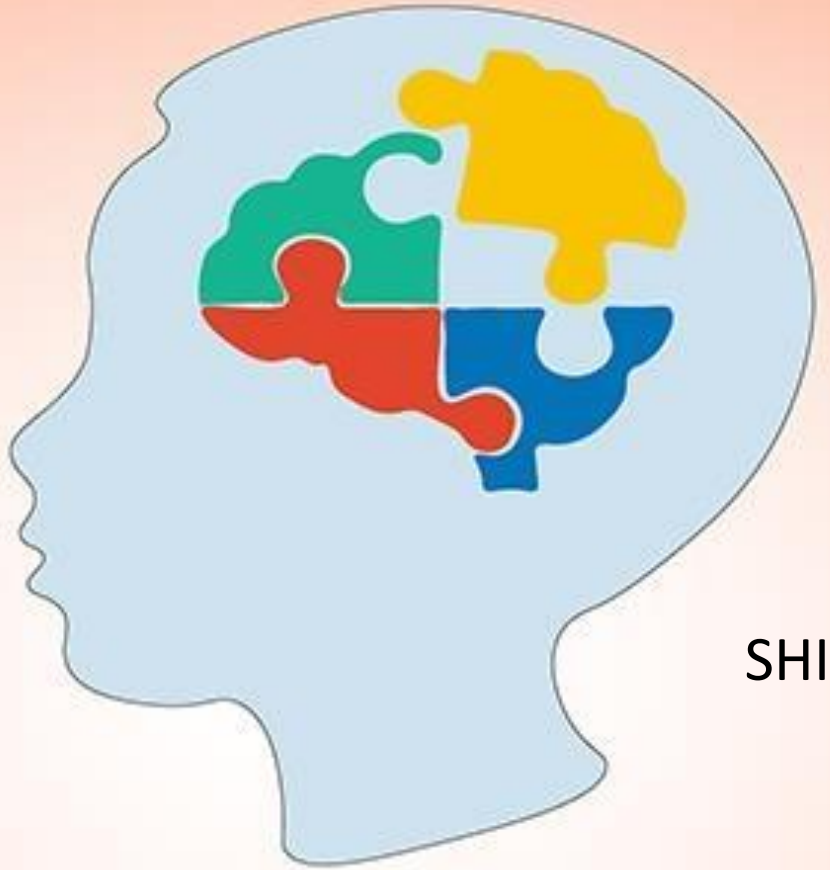
TREATMENT OF AUTISTIC SPECTRUM DISORDER



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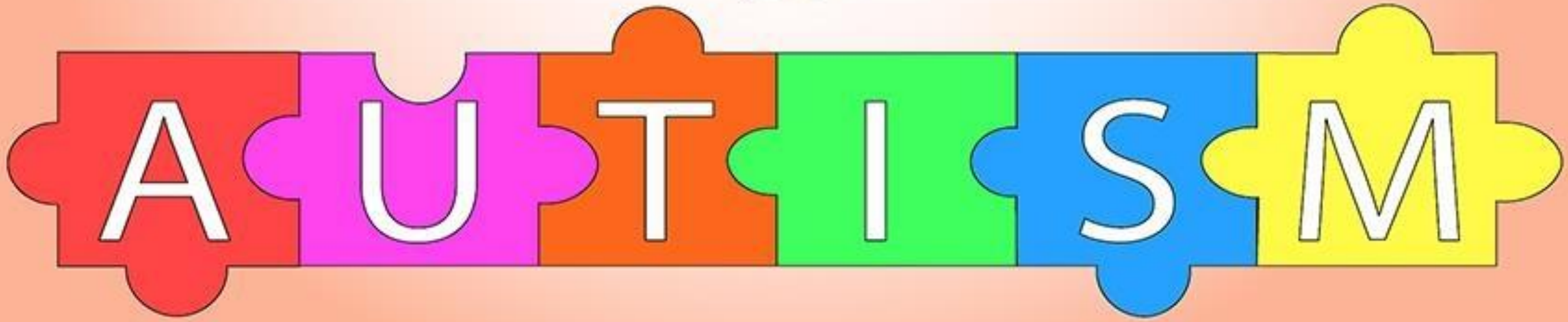
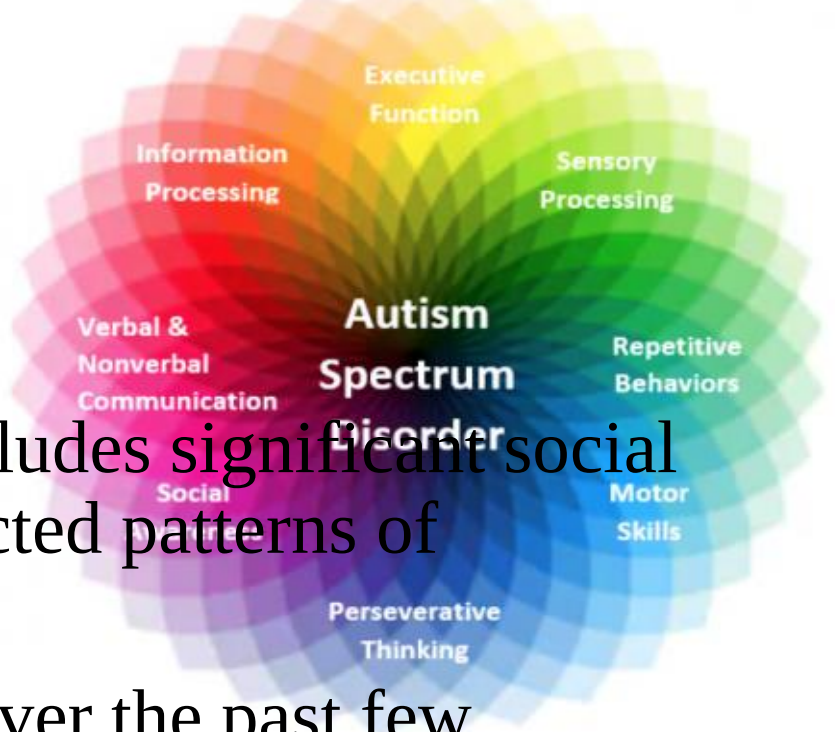
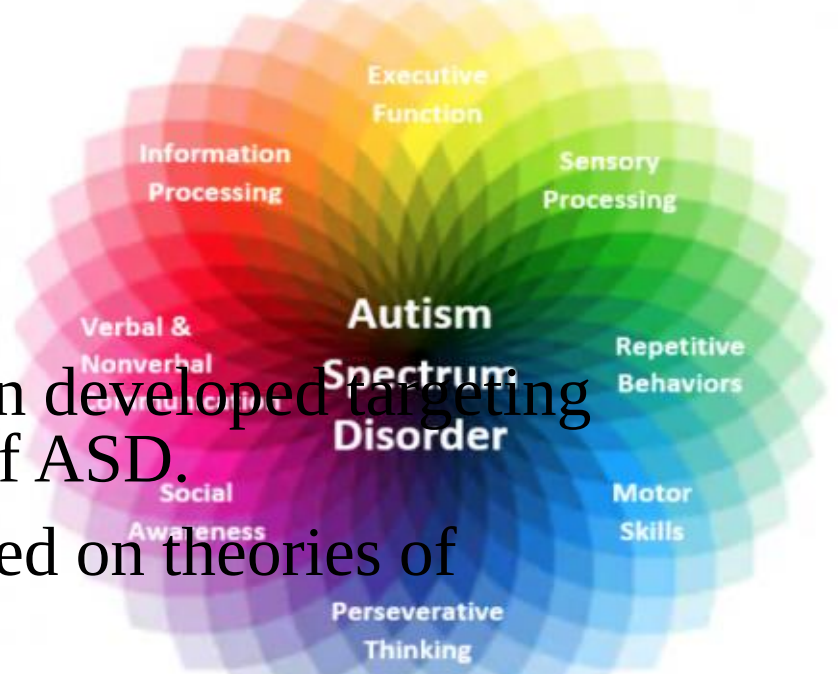


AUTISM



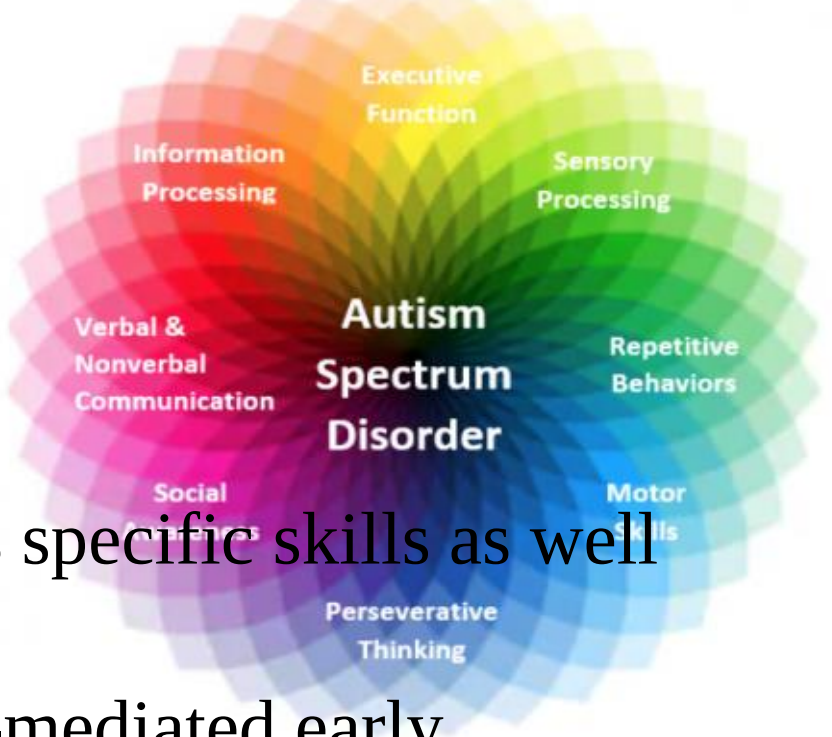
- Autism spectrum disorder is a diagnosis that includes significant social communication deficits/delays along with restricted patterns of interests and behaviors.
- The prevalence of this diagnosis has increased over the past few decades, and it is unclear whether this is solely attributable to the increased awareness of milder forms of the disorder among medical providers

Psychosocial Therapies



- Many different psychosocial interventions have been developed targeting both the core symptoms and associated symptoms of ASD.
- Applied behavior analysis (ABA) is a treatment based on theories of learning and operant conditioning.
- It includes specific intervention targets, coupled with positive reinforcement (verbal praise, tokens, or edible rewards), with repetition of learning-trials a key component
- A meta-analysis examining the efficacy of ABA interventions for young children with autism showed medium to large positive effects on intellectual functioning, language development, daily living skills acquisition, and social functioning, with the larger effect sizes observed on language-related outcomes

Psychosocial Therapies

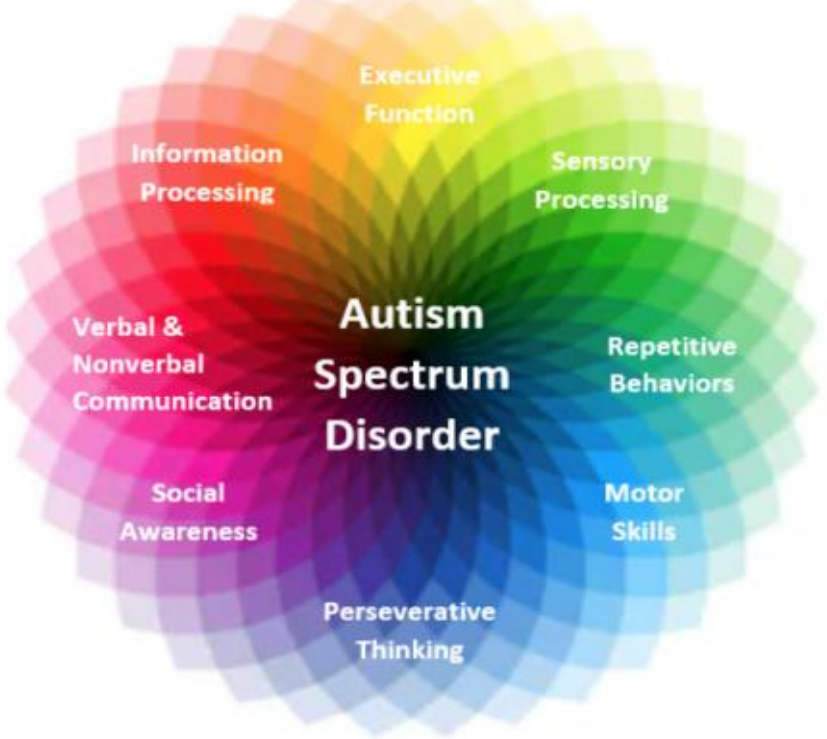


- Pivotal Response Treatment (PRT) and includes

a more naturalistic behavioral method that targets specific skills as well as motivations

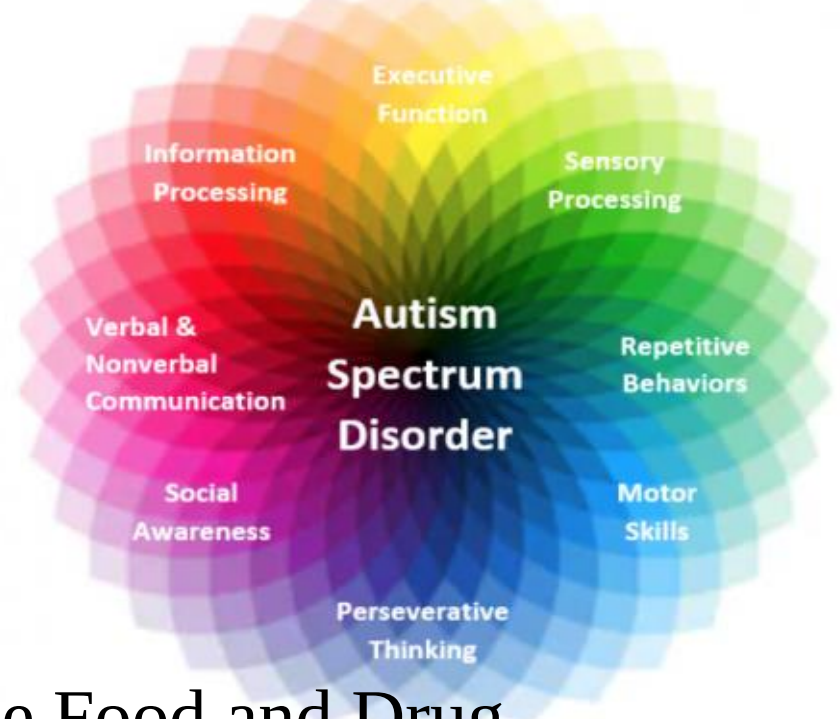
- Other psychosocial interventions include parent-mediated early interventions (teaching parents interventions that they can then apply in the home) and social skills interventions.
- Cognitive behavior therapy (CBT) has been studied as a treatment for co-morbid anxiety disorders in children and adolescents with autism spectrum disorder.

Pharmacology



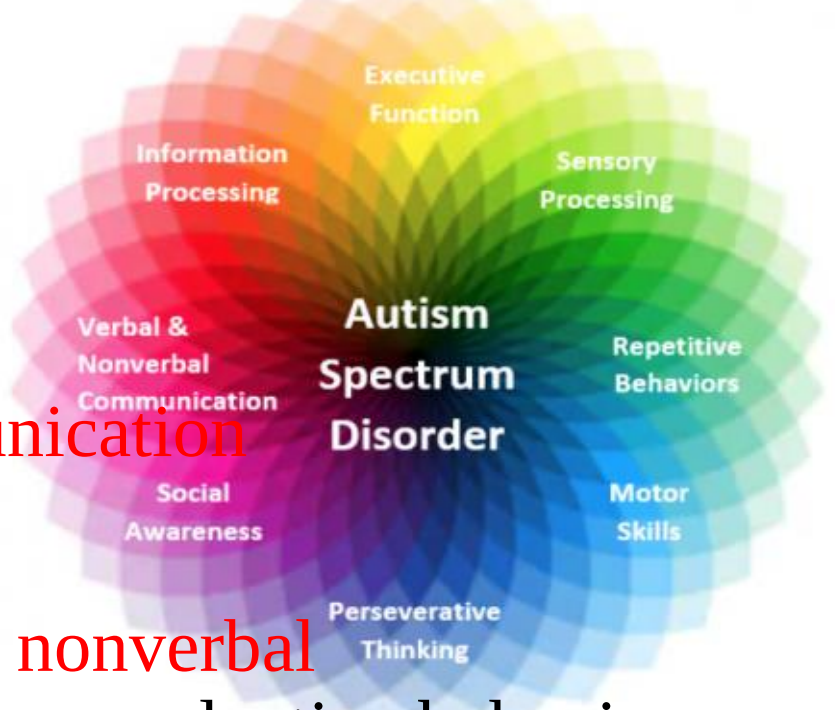
Medications are primarily used for treating associated symptoms of autism spectrum disorder, as efficacy for use in treating the core symptoms of autism has not been established

Atypical Antipsychotics



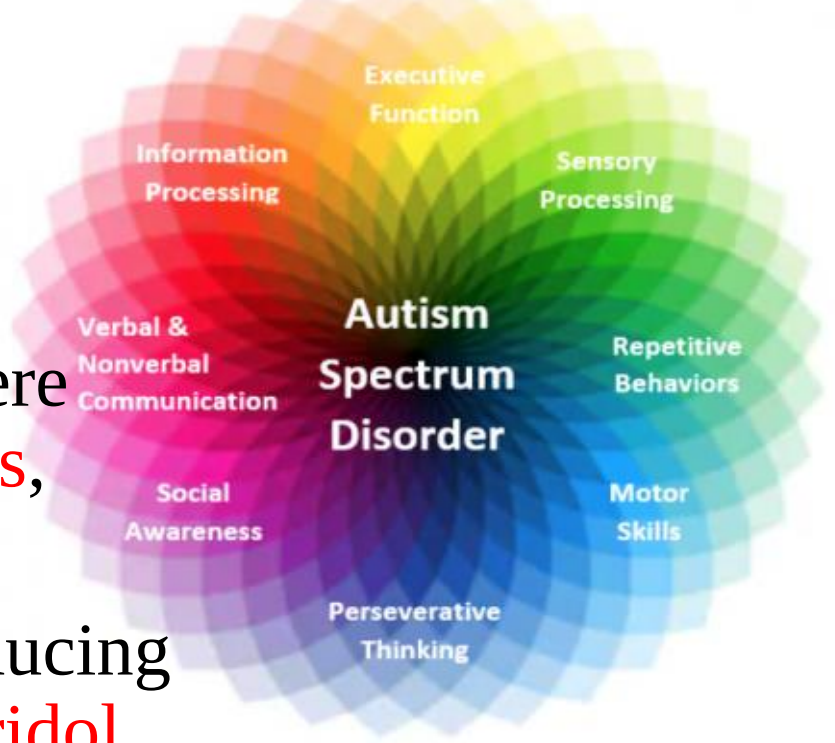
- Risperidone and aripiprazole are approved by the Food and Drug Administration (FDA) for the treatment of irritability associated with the diagnosis of autism spectrum disorder.
- Risperidone is approved in children at least 5 years of age
- and aripiprazole is approved for children at least 6 years of age.

Risperidone



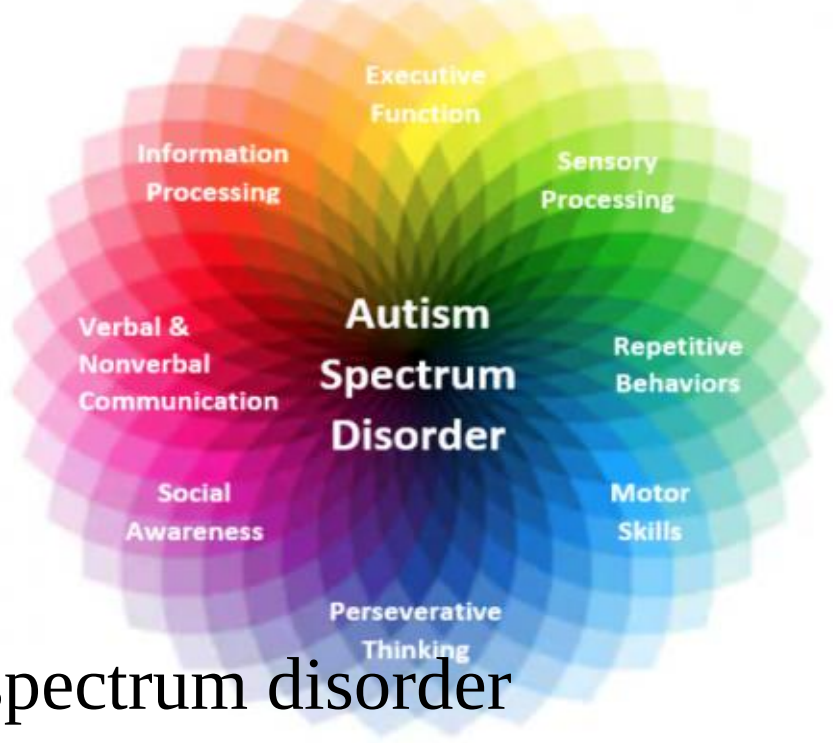
- social and emotional responsiveness and communication aggressiveness, hyperactivity, and irritability
- Risperidone improves social responsiveness and nonverbal communication a long with direct positive effects on adaptive behavior
- treating irritability associated with autism defined as ≥ 25% decrease in the irritability score
- Of the responders in the risperidone group, 68% maintained this response at a 6 month follow up.

Risperidone



- Significant side effects in the risperidone group were weight gain, increased appetite, fatigue, drowsiness, dizziness, transient dyskinesias and drooling.
- Risperidone was shown to be more effective in reducing behavioral symptoms and impulsivity than haloperidol.
- When comparing adverse effects, the risperidone group had greater increases in prolactin and the haloperidol group had greater increases in alanine amino transferase (ALT).

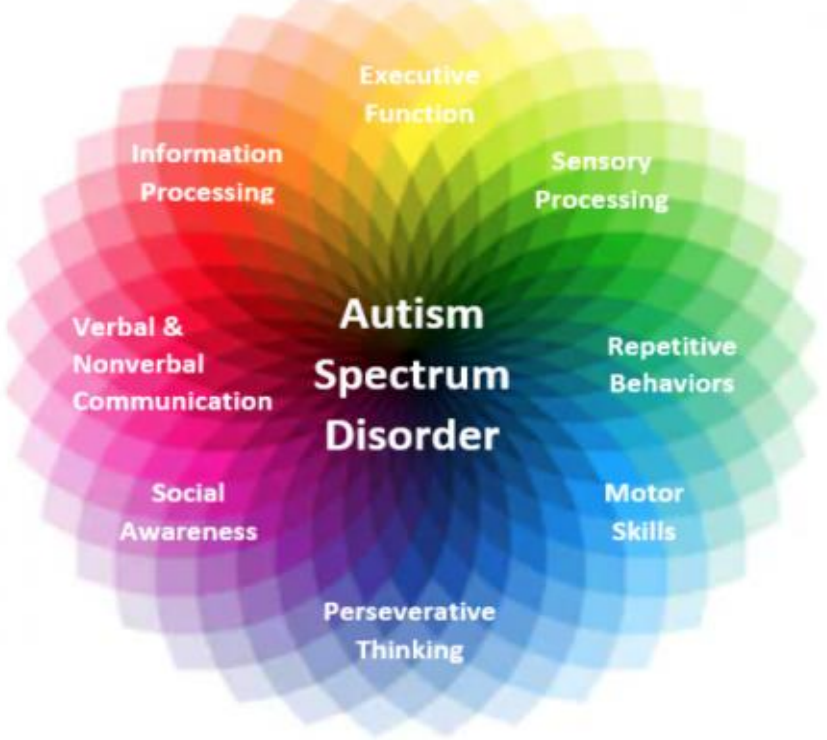
Aripiprazole



- Treatment of irritability associated with autism spectrum disorder

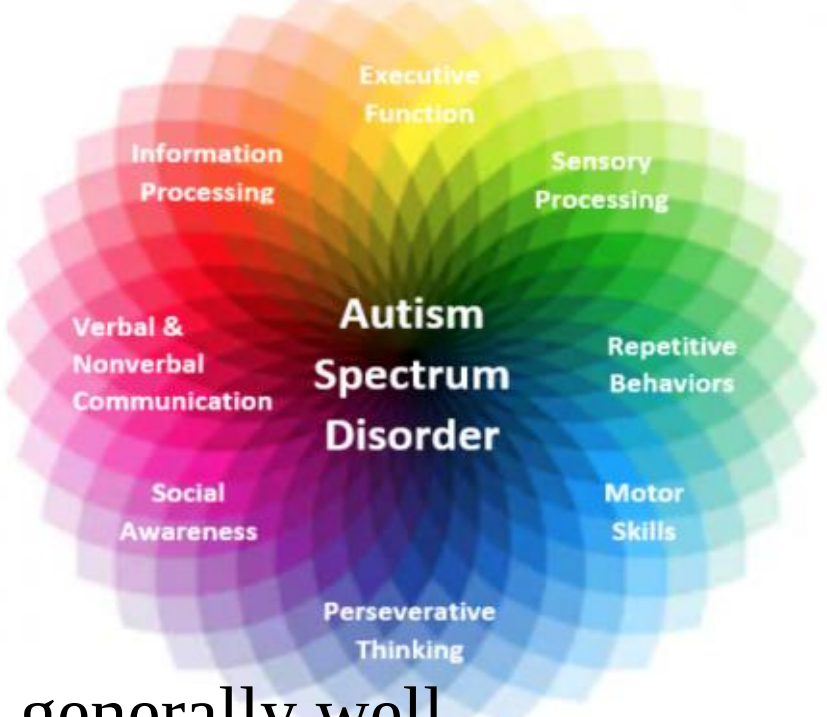
- The most common side effects included weight gain, vomiting, nasopharyngitis, appetite increase, pyrexia, upper respiratory tract infection, and insomnia.

Olanzapine



- irritability, hyperactivity, and excessive speech
- Significant weight gain was observed (mean 4.7 kg), along with appetite increase and loss of strength.

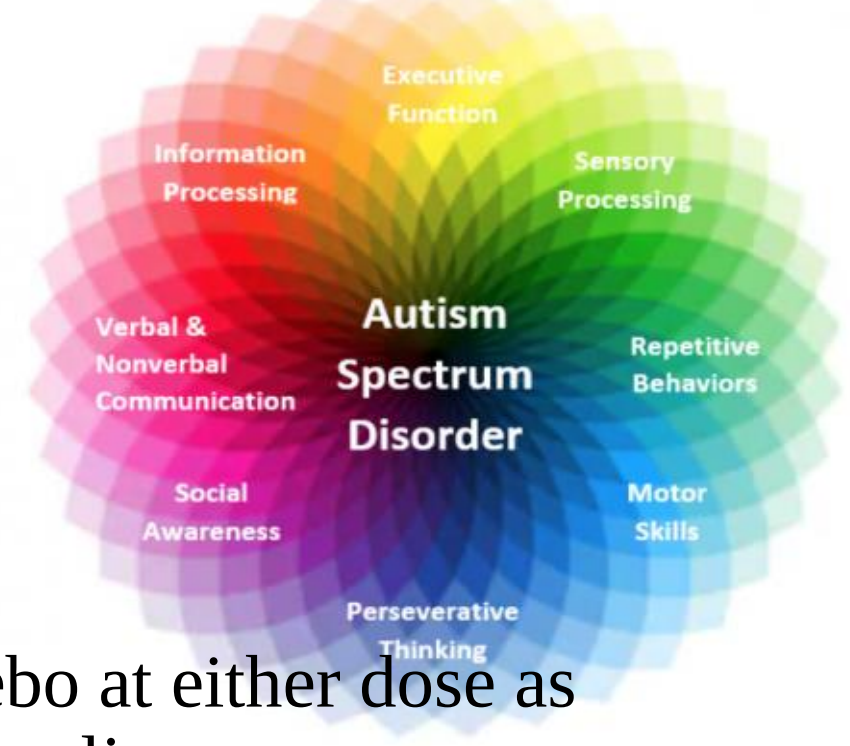
Quetiapine



- Significant improvements in aggression and sleep, generally well-tolerated at low doses.

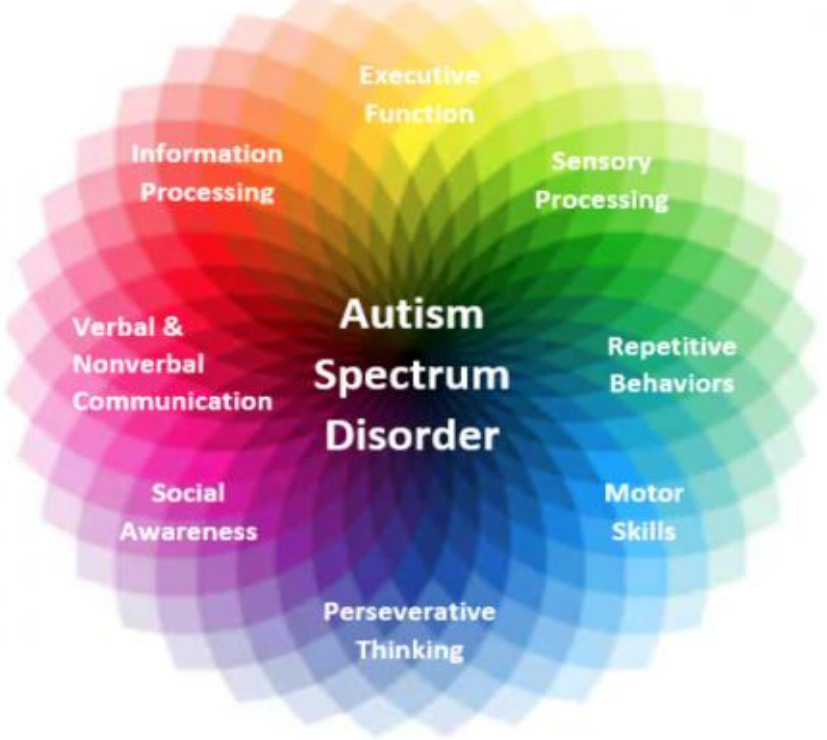
- Side effects with quetiapine were sedation, a possible seizure, increased appetite and weight gain.

Lurasidone



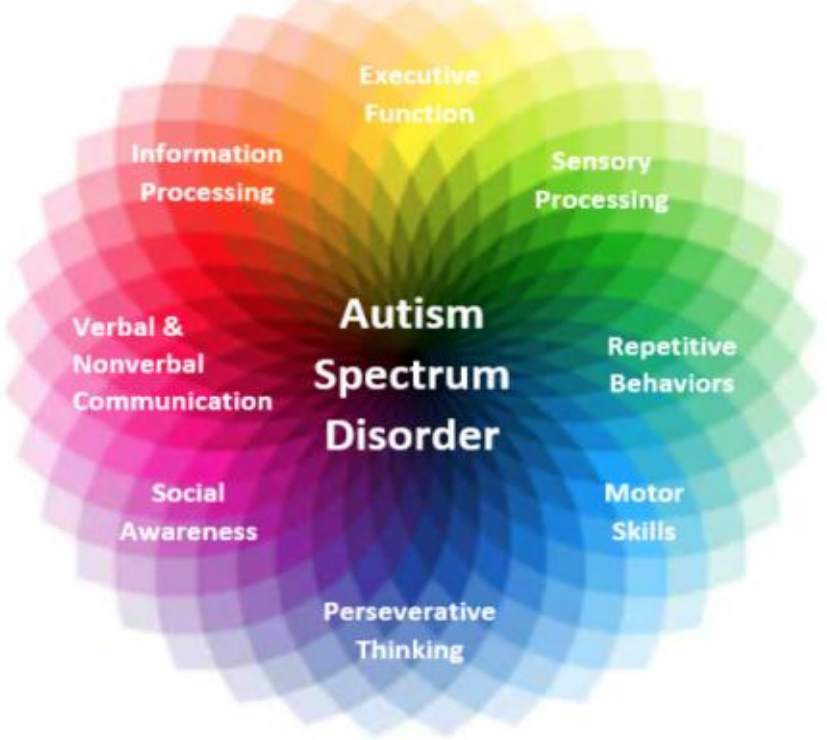
- Contarovertial
- Lurasidone was not found to be superior to placebo at either dose as measured by the change in ABC-I scores from baseline.
- Lurasidone , superior to placebo, as measured by change in the CGI-I scores from baseline to endpoint,
- The most commonly observed side effects included vomiting and somnolence.

Ziprasidone



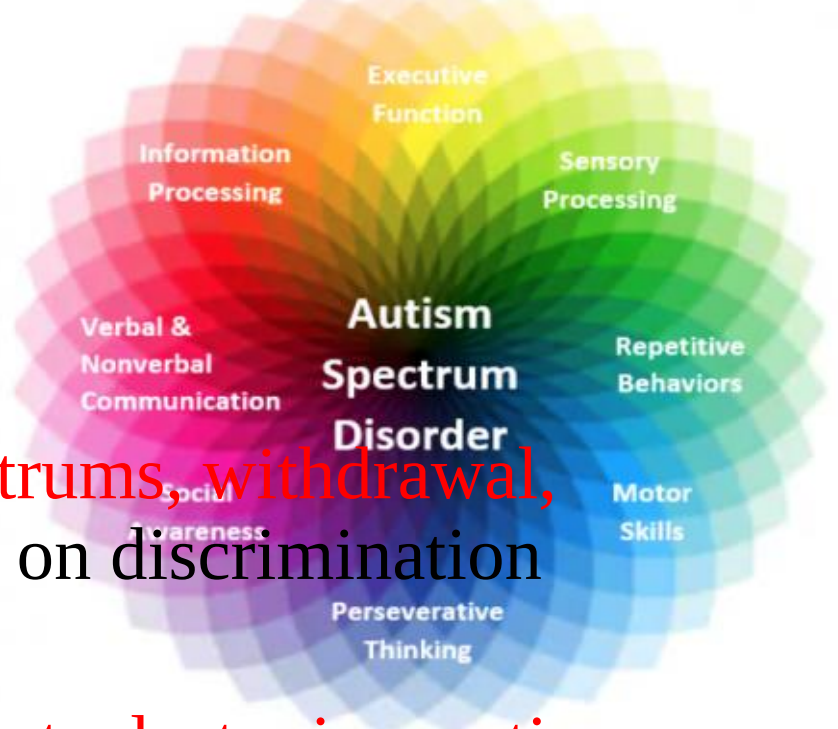
- well-tolerated, with no weight gain
- mean QTc increase of 14.7 msec.
- Responding in autism or pervasive developmental

Paliperidone



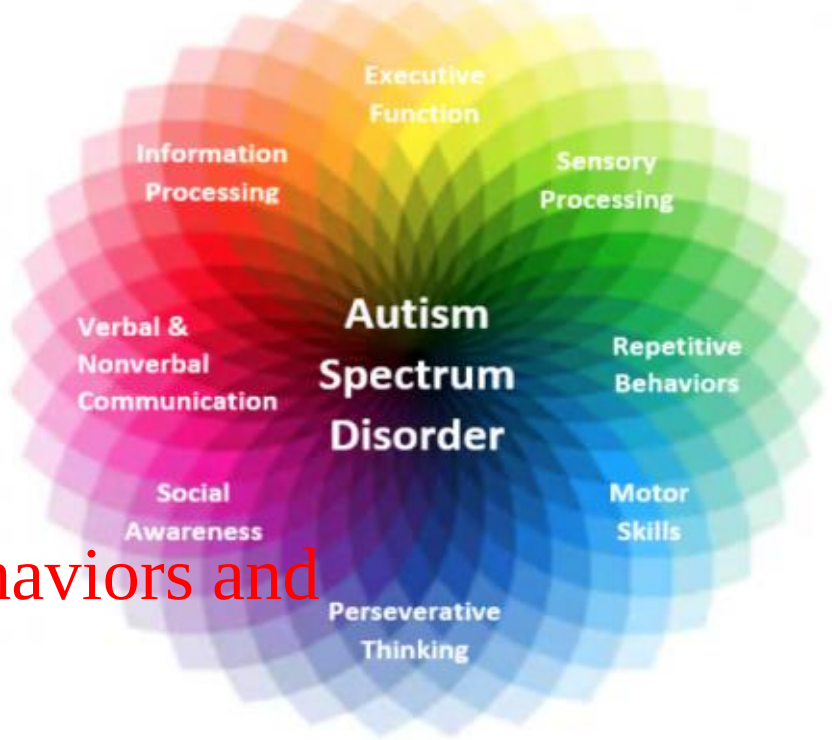
- Treatment of irritability
- Mild to moderate extrapyramidal symptoms

Typical Antipsychotics



- Haloperidol
- benefits in the areas of hyperactivity, temper tantrums, withdrawal, stereotypical behaviors, and facilitating learning on discrimination tasks
- side effects included sedation, irritability, and acute dystonic reactions, withdrawal or tardive dyskinesia
- The risk of dyskinesia increased with length of treatment, making long-term use of this medication especially concerning.
- For this reason, haloperidol should be considered after the atypical antipsychotics

Antidepressants

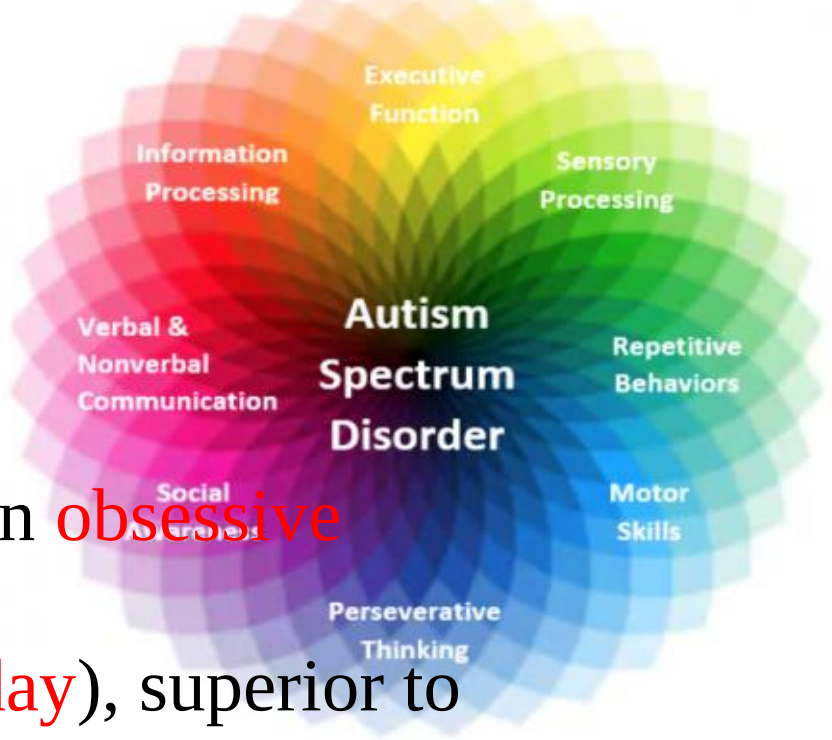


- Treatment of symptoms of repetitive, ritualistic behaviors and insistence on restricted patterns of routines.
- Selective serotonin reuptake inhibitors (SSRIs),
- Tricyclic antidepressants,
- other antidepressants

Selective Serotonin Reuptake Inhibitors (SSRIs)

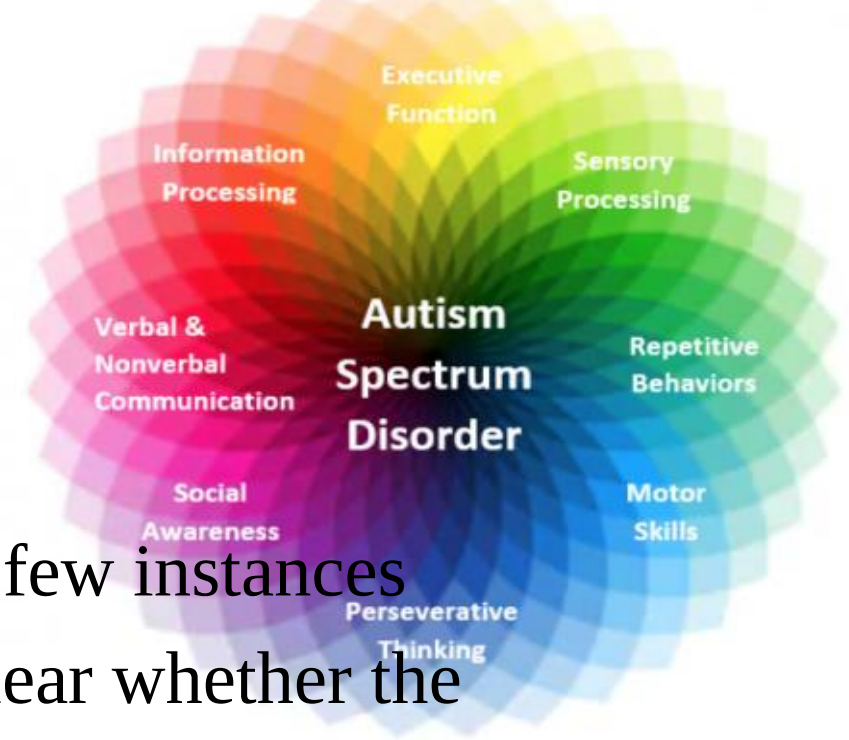
- Reduction of ritualistic behavior, anxiety, and aggression,
- as well as behavioral rigidity, obsessive-compulsive disorder and stereotypies
- Efficacy of SRIs may be moderated by age, with better responsivity in adults than in children.
- Evidence for possible developmentally sensitive altered regulation of serotonin synthesis in autistic children
- rationale for giving serotonergic drugs to very young autistic children to improve synaptic plasticity during periods of brain development.

Fluoxetine



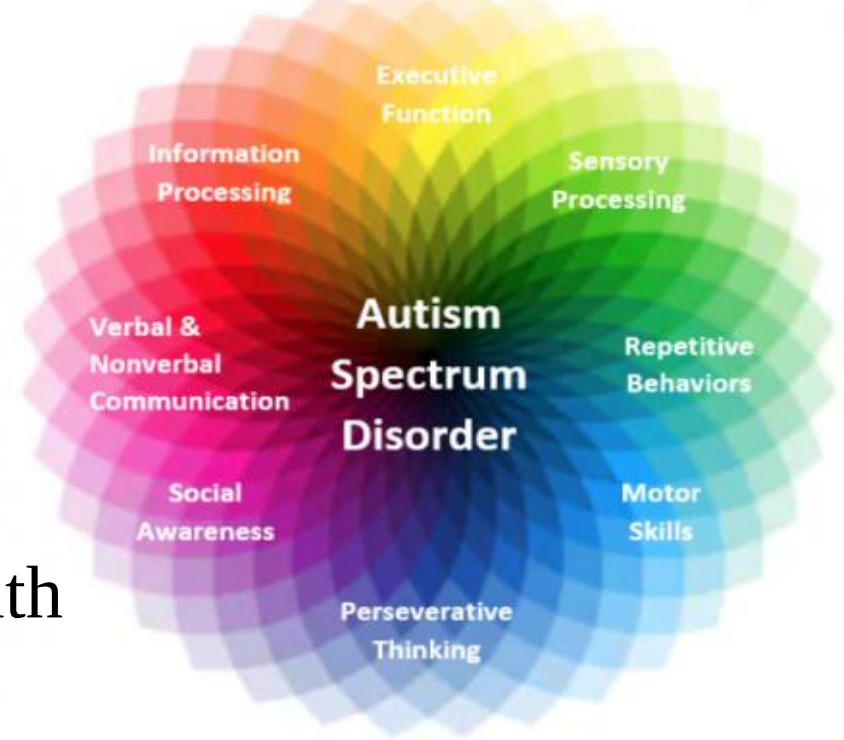
- fluoxetine demonstrated significant improvement in obsessive behaviors and anxiety
- Low-dose liquid fluoxetine (mean dose of 10 mg/day), superior to placebo on a measure of repetitive behaviors
- fluoxetine demonstrated significant improvement in obsessive behaviors and anxiety, and PET scans demonstrated fluoxetine-elevated metabolic rates in the right frontal lobes
- Fluoxetine showed conflicting results
- Observed side effects were restlessness, hyperactivity, agitation, decreased appetite or insomnia.

SRI



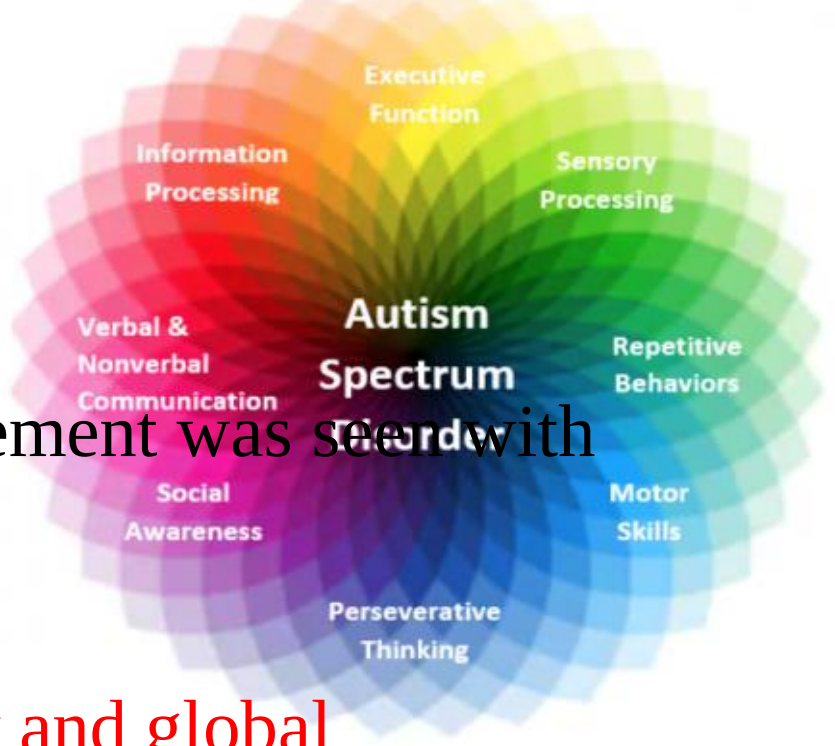
- Seizures have emerged under SRI treatment in a few instances
- although this is a seizure-prone population not clear whether the medications were causal.
- Concern about reports of an association of fluoxetine and possibly other selective SRIs with suicidal ideation in depressed children,
- FDA has recommended that children on these medications should be very carefully monitored

Citalopram



- Citalopram was not superior to placebo in a randomized, placebo-controlled trial of 149 children and adolescents (aged 5 to 17 years) with autism spectrum disorder.
- 97% of those in the citalopram group experienced adverse effects, including increased energy, impulsivity, decreased concentration, hyperactivity, stereotypy, diarrhea, insomnia, and dry skin or pruritus.

SRI

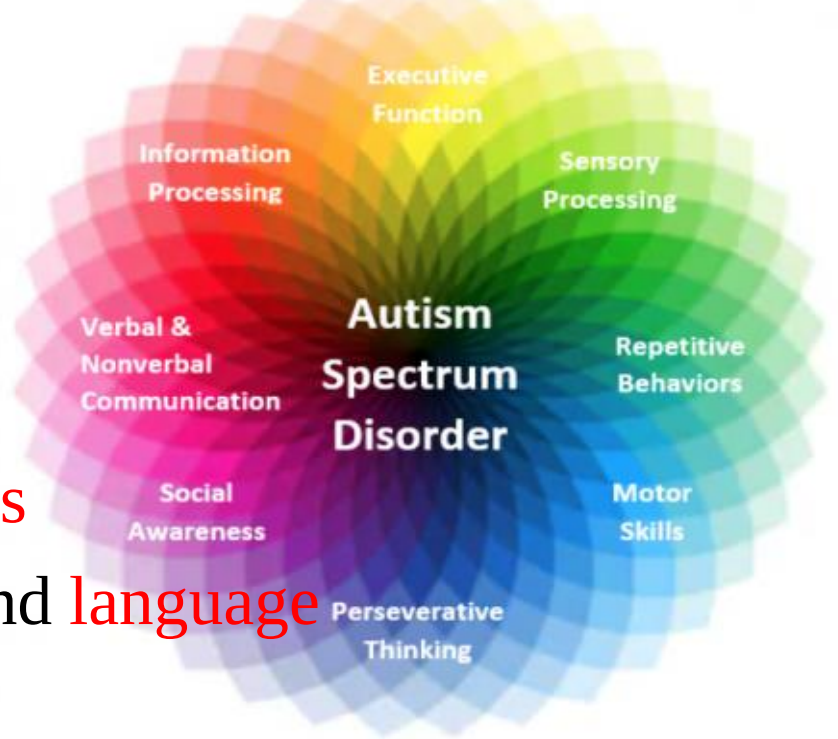


- Fluvoxamine had no significant clinical improvement was seen with the medication when compared to placebo.

Escitalopram

- Significant improvement was seen on irritability and global improvement measures, and the study highlighted the need to start with very low doses and titrate slowly.
- The most commonly reported adverse effects were irritability and hyperactivity, which appeared dose-related.

Other Antidepressants

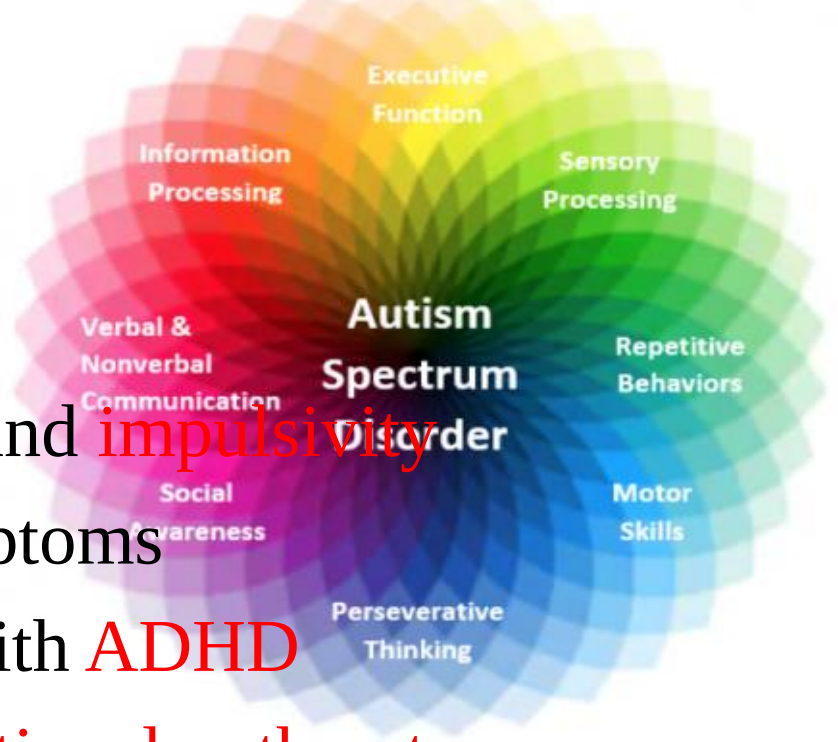


- Low dose venlafaxine ,effective for repetitive behaviors

and restricted interests, social deficits, communication and language function, inattention, and hyperactivity

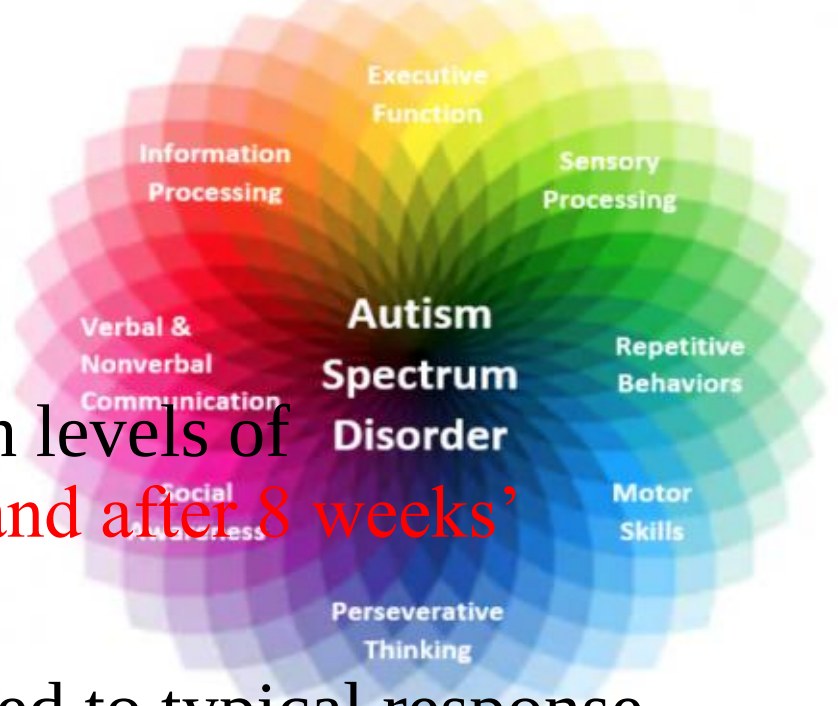
- adverse effects :behavioral activation, nausea, inattention and polyuria.
- Mirtazepine was not effective for symptoms of ASD
- Clomipramine was superior to both placebo and desipramine on measures of stereotypical behaviors, anger, and compulsive, ritualized behaviors.
- Both clomipramine and desipramine :reducing hyperactive behaviors.
- Side effects ,acute urinary retention, requiring catheterization, but relatively well-tolerated

Stimulants



- Methylphenidate for inattention, hyperactivity, and impulsivity
- superior to placebo in treating hyperactive symptoms
- Adverse effects more frequently than patients with ADHD
- appetite decrease, insomnia, irritability and emotional outbursts
- Modest effects and side effects ,concerning, especially at higher doses
- a need to start these medications at low doses and increase slowly.
- Doses at the 0.25 and 0.5 mg/kg level were effective in reducing hyperactivity and impulsivity, but less effective in reducing inattention

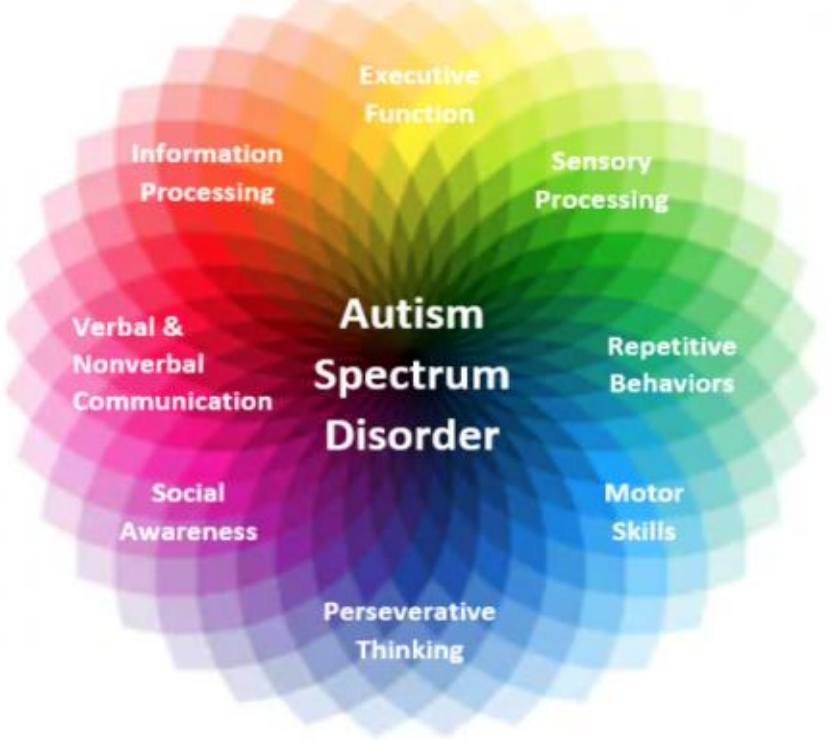
Stimulants



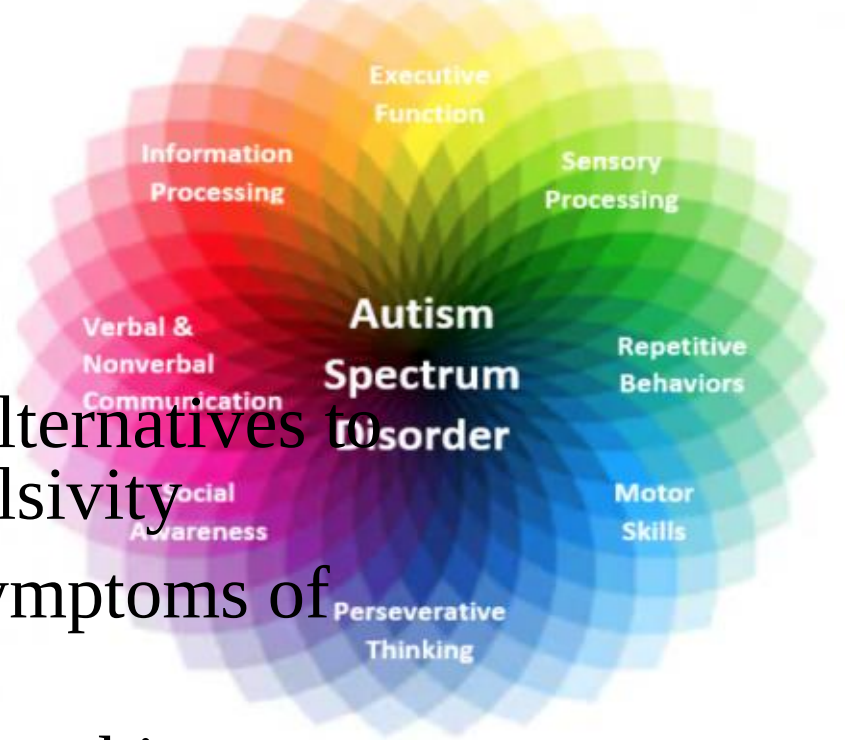
- methylphenidate in children with ASDs and high levels of hyperactivity and/or impulsiveness, at 4 weeks and after 8 weeks' continuation.
- The response rate was about 35 percent compared to typical response rates of around 70 percent in non-PDD children with ADHD.
- Common side effects : decreased appetite and trouble falling asleep.
- benefits of methylphenidate extended to some aspects of social interactions, self-regulation, and affect

Atomoxetine

- Modest improvements in hyperactive and impulsive symptoms were seen in these studies, and atomoxetine was generally well-tolerated
- effective in some core autism symptoms (decreasing restricted and stereotyped behaviors and communication) but showed no effect on social functioning



Alpha-2 agonists

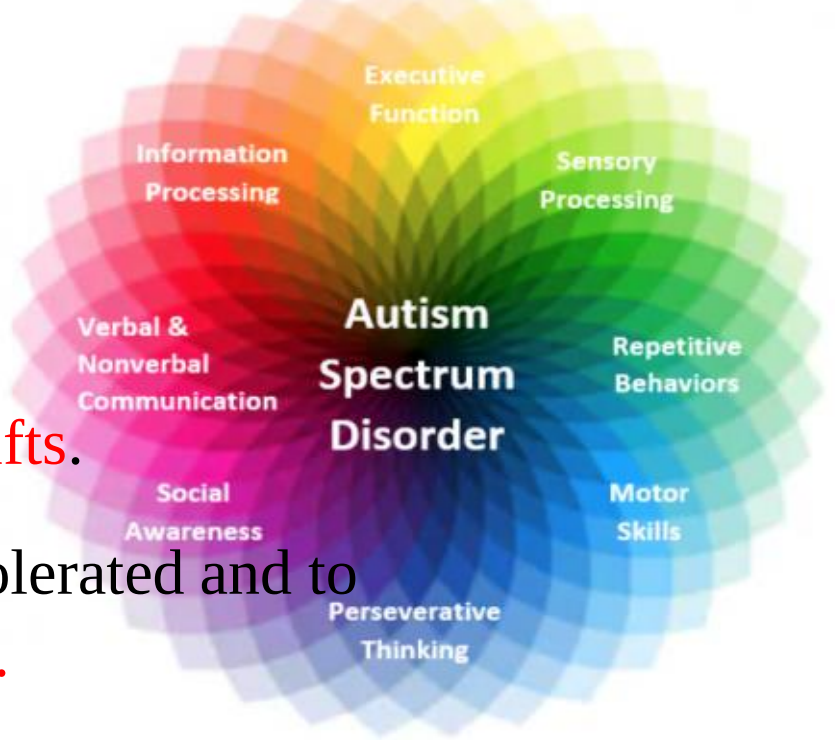


- alpha-2 agonists have been studied as possible alternatives to stimulants for managing hyperactivity and impulsivity
- Clonidine to be at least modestly effective for symptoms of hyperactivity.
- helpful for other symptoms, such as social relationships, sensory responses, irritability, sleep and aggression.
- Adverse effects : sedation or drowsiness, but otherwise well-tolerated.
- extended-release guanfacin superior to placebo on measures of hyperactivity and global improvement.
- Blood pressure decreased slightly early in the study,

Naltrexone

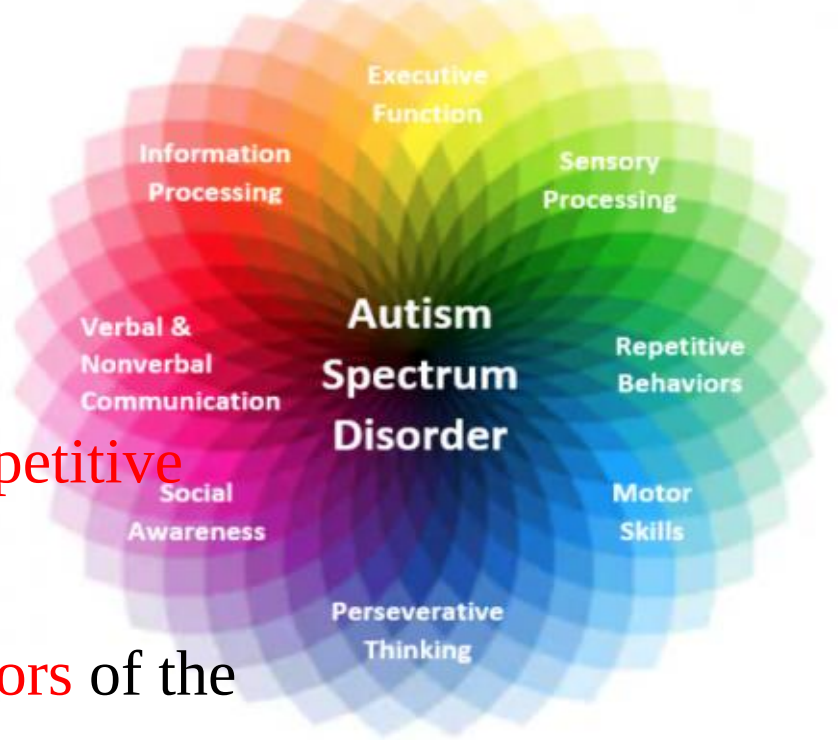
- Reducing hyperactivity and impulsivity
- Core symptoms did not appear to improve
- Autism : associated with hypersecretion of brain opioids, beta-endorphins,
- Many symptoms of autism are similar to opiate administration,
- such as decreased socialization, repetitive stereotypic movements, and motor hyperactivity
- Side effects were mild gastrointestinal symptoms, appetite decrease, and drowsiness ,in some, stereotypic behaviors were increased.

Antiepileptic Drugs



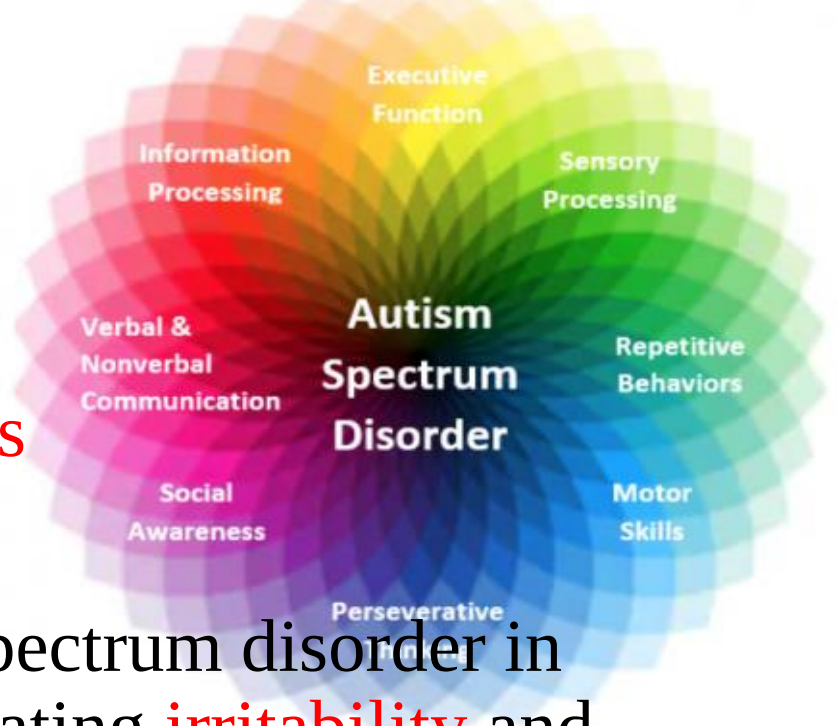
- antiepileptic, particularly for treating intense rapid mood shifts.
- Levetiracetam and divalproex sodium appeared to be well tolerated and to improve repetitive behavior, impulsivity, and mood stability.
- Topiramate in children and adolescents with ASDs reduced misconduct, hyperactivity, and inattention.
- Lamotrigine was not better than placebo on disruptive behavior and autism symptoms
- levetiracetam, no difference from placebo on measures of behavioral disturbance, repetitive behavior, and autism

Antiepileptic Drugs



- Divalproex sodium was better than placebo in decreasing repetitive behavior
- Patients with the most robust response had repetitive behaviors of the compulsive type, as opposed to stereotypies.
- It has been hypothesized that the mechanism of benefit from these medications might be their effect on subclinical seizures, reported to occur in this population.
- no controlled trials investigating whether treatment with anticonvulsants in children with autism who have epileptiform discharges but no clinical seizures might improve behavioral outcomes in children with autism

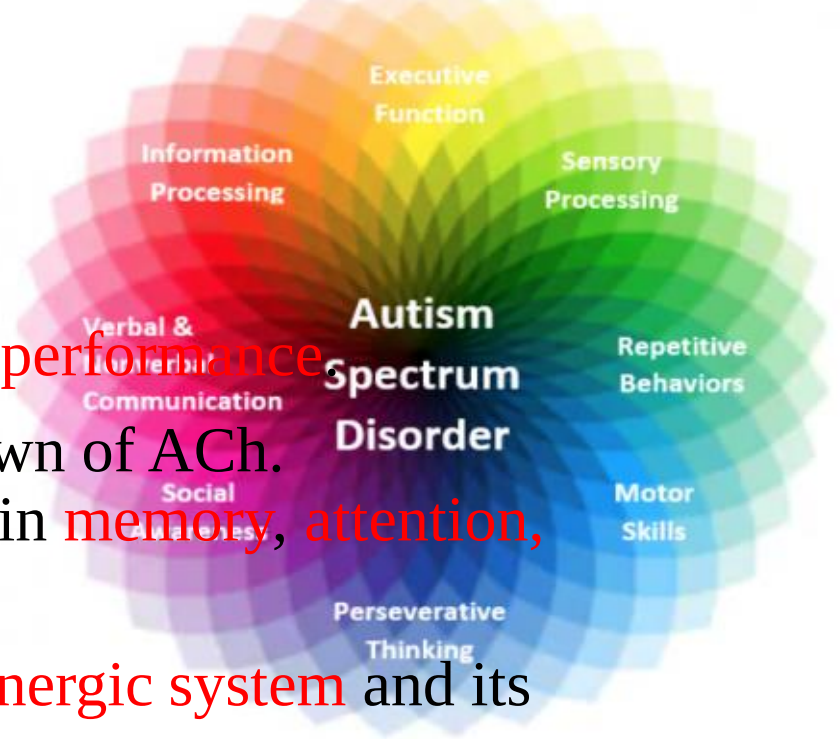
Mood Stabilizers



- particularly for treating intense rapid mood shifts

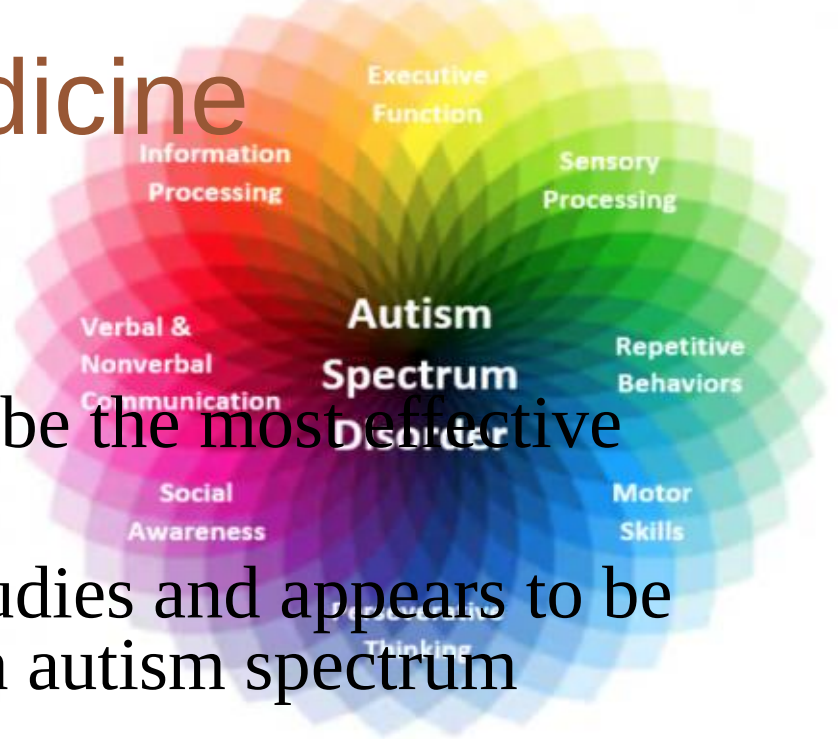
- divalproex sodium for the treatment of autism spectrum disorder in children and adolescents, had the efficacy in treating irritability and improving repetitive behaviors
- The most common adverse effect in the divalproex sodium group was irritability.
- no significant difference between lamotrigine and placebo on any of the outcome measures

Cholinesterase Inhibitors



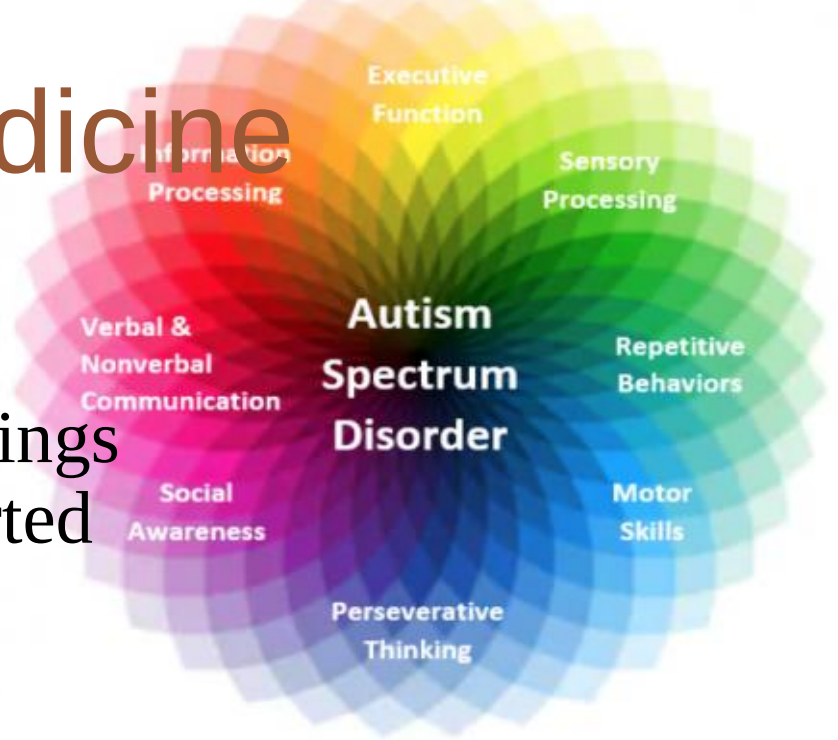
- Acetylcholine ,a significant role in attention and memory performance.
- Acetylcholinesterase inhibitors (AChE) slow the breakdown of ACh. cholinesterase inhibitors, such as donepezil, slow decline in memory, attention, and learning in Alzheimer's disease.
- postmortem studies have found abnormalities of the cholinergic system and its nicotinic receptors in the brains of in autism
- potential benefit of these drugs in ameliorating neurodevelopmental disorders
- donepezil in improvements in irritability and hyperactivity, but memory and attention were not measured
- Galantamine may be beneficial for irritability, hyperactivity and social withdrawal associated with autism spectrum
- The efficacy of cholinesterase inhibitors is yet to be demonstrated

Complementary Alternative Medicine



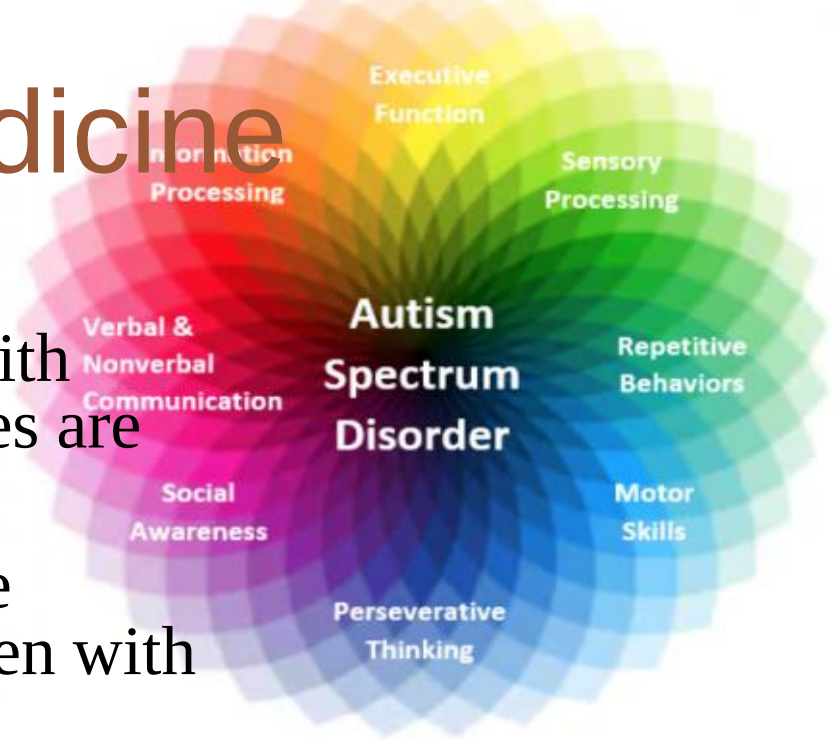
- combination treatment (melatonin plus CBT) to be the most effective intervention for sleep-related difficulties
- Melatonin was well-tolerated in all the above studies and appears to be a safe treatment option for sleep in children with autism spectrum disorder.
- Omega-3 fatty acids have been examined as potential treatments for autism spectrum disorder, specifically for the associated symptom of hyperactivity.
- Methyl B12 has been studied in two randomized, placebo-controlled trials as a treatment for both behavioral symptoms and core symptoms of autism spectrum disorder in children

Complementary Alternative Medicine



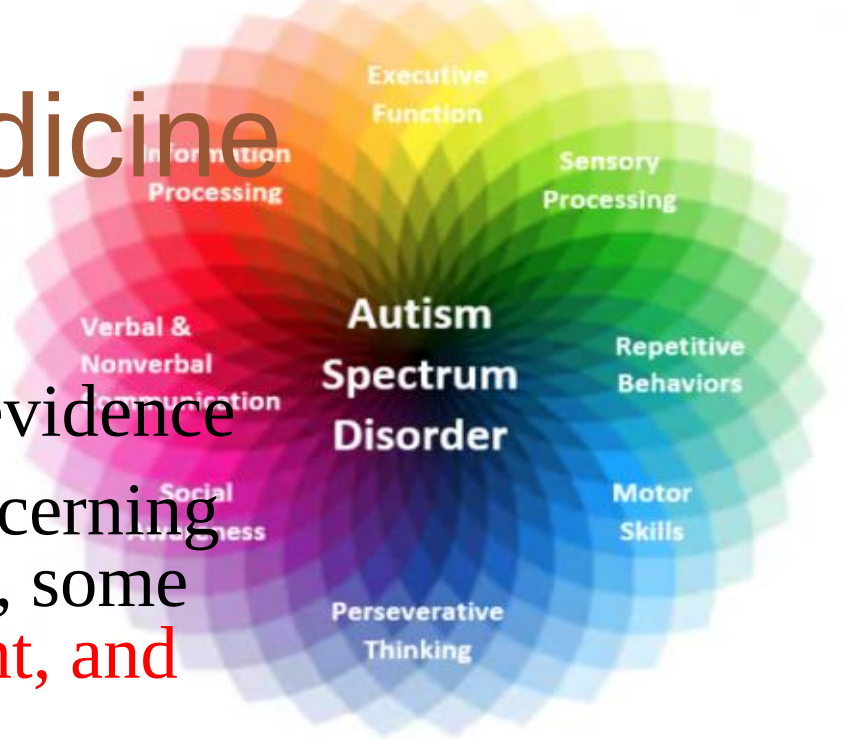
- Amantadine showed no improvement on parent-ratings of hyperactivity and irritability, but clinicians reported significant improvements in behavioral ratings
- augmenting agents to risperidone and haloperidol include pentoxifylline, N-acetylcysteine, riluzole, memantine, amantadine, celecoxib, pioglitazone, and buspirone.
- Cyproheptadine was studied in combination with haloperidol and was found to be superior to haloperidol plus placebo

Complementary Alternative Medicine



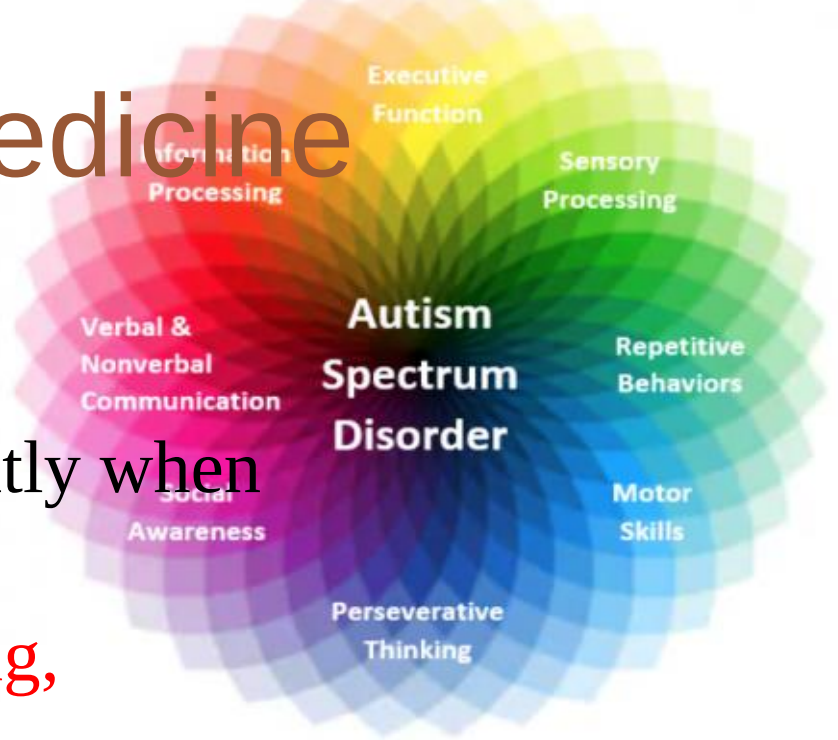
- N-acetylcysteine may improve irritability in children with autism and appears to be well tolerated, but more studies are needed
- gluten-free/casein-free diet suggested no change in core symptoms or associated behavioral symptoms in children with autism in a double-blind challenge trial
- Intravenous immunoglobulin therapy has been suggested as a potential treatment for autism spectrum disorder, however there are no randomized-controlled trials
- there is significant risk associated with this treatment, therefore, available evidence does not support this treatment for ASD.

Complementary Alternative Medicine



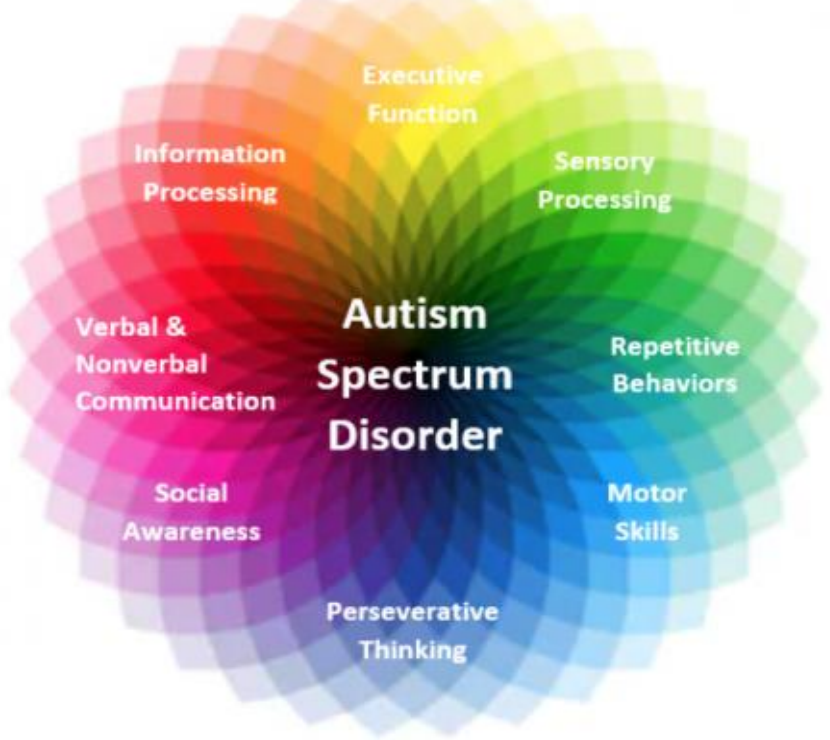
- Chelation associated with significant risks ,limited evidence
- A small group showed worsening of symptoms, concerning here are risks associated with unnecessary chelation, some of which are severe (hypocalcemia, renal impairment, and reported death),
- FDA released a warning for parents regarding several possibly harmful treatments that do not have evidence including:
- Chelation therapies, hyperbaric oxygen therapy, miracle mineral solution, detoxifying clay baths, and coconut kefir and other probiotic products.

Complementary Alternative Medicine



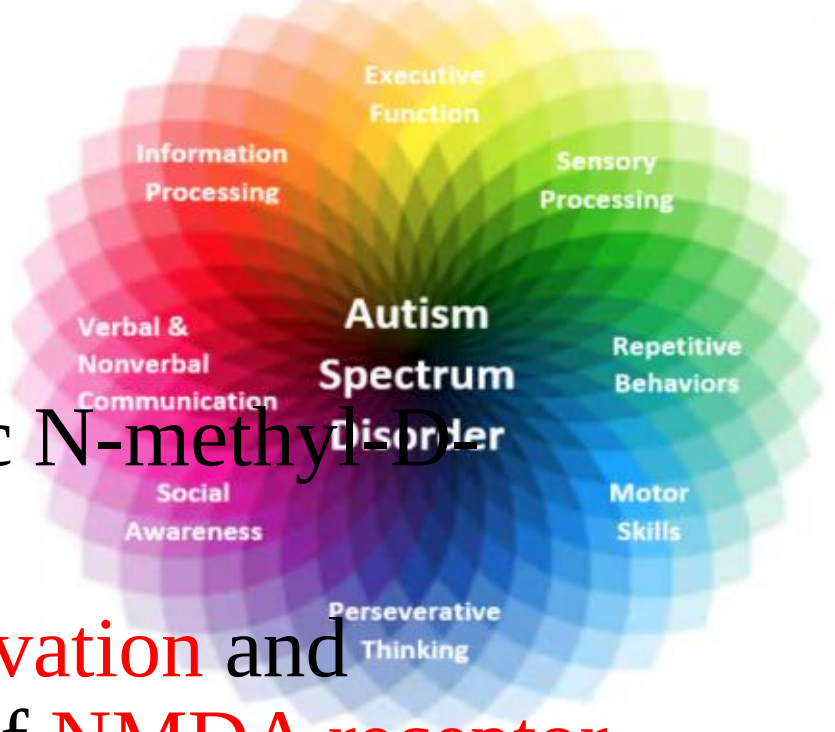
- oxytocin to improve emotion recognition significantly when compared to placebo
- levocarnitine (l-carnitine), and the GABA-ergic drug, bumetanide.
- vitamin B6 and magnesium concluded that the few studies available were inconclusive
- Melatonin therapy has been used to treat the sleep disturbances in ASD, based on low plasma levels or urinary excretion of melatonin

CBD, Cannabidiol



- 5-HT1A receptor agonist,
- which might facilitate anxiolytic effects.
- Its presumed antipsychotic effect is attributed to partial agonism at dopamine D2 receptors,
- similar to the antipsychotic action of aripiprazole
- and has been associated with enhanced social behavior in multiple studies

Memantine

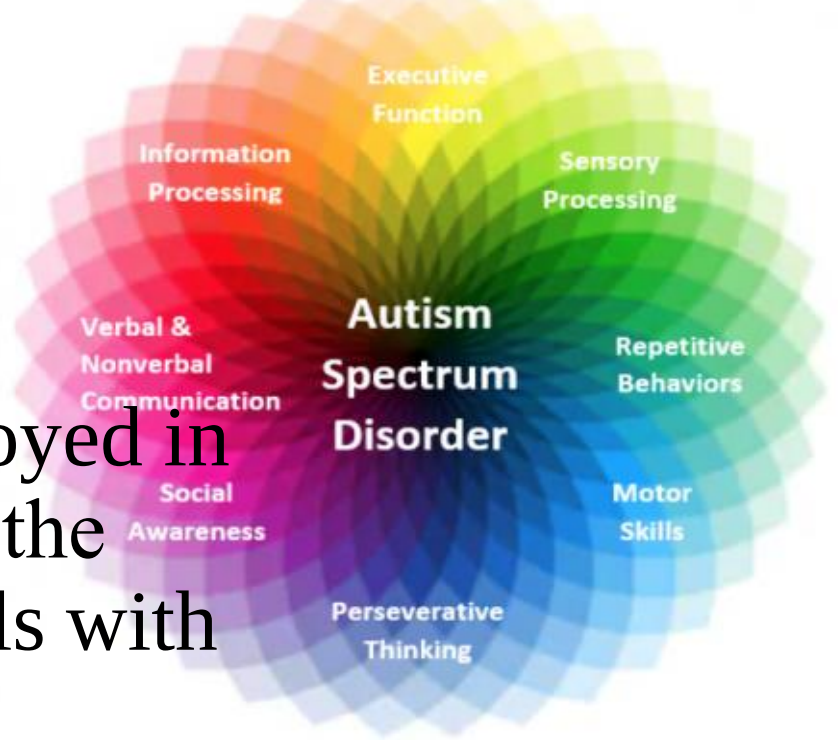


Noncompetitive antagonist of glutamatergic N-methyl-D-aspartate (NMDA) type receptors.

It works by inhibiting pathological overactivation and subsequent neuroexcitation and cell death of NMDA receptor cells by glutamate - an amino acid normally found in the brain.

Individuals with ASD have been reported to have pathologically increased activity levels of glutamate and NMDA receptors, hence the aim to modulate this biochemical effect, and potentially ameliorate the clinical symptoms of ASD.

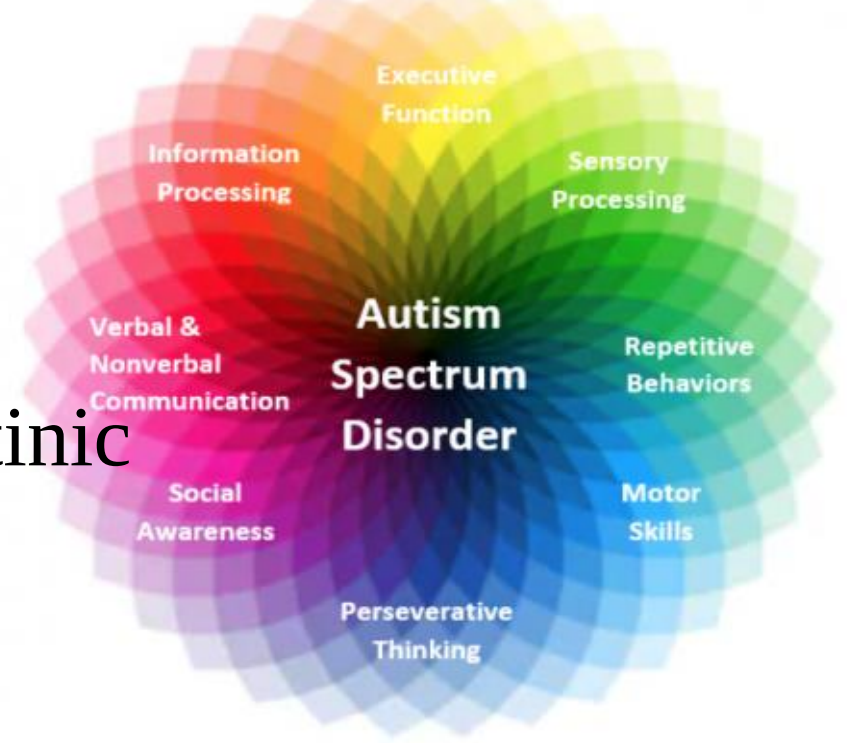
Memantine



This property of memantine has been employed in the treatment of Alzheimer's disease and is the basis for trials in the treatment of individuals with ASD

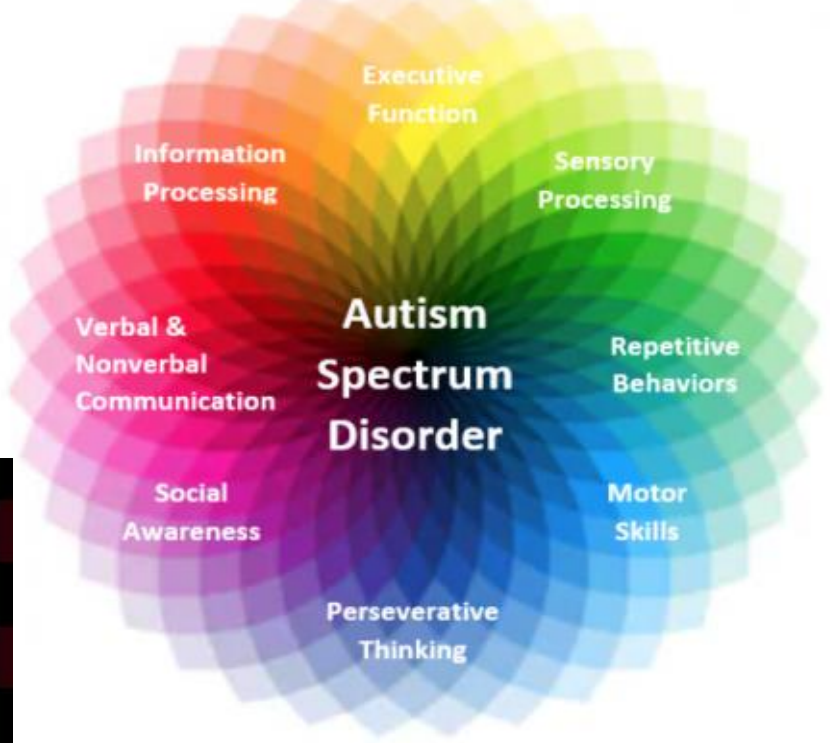
The exact mechanism ,unclear, but it is thought that inhibition of 5-HT(3) receptors by memantine might improve cognition and learning and reduce anxiety, either by increasing circulating serotonin levels or preventing receptor activation and glutamate release

Memantine



- also a non-competitive antagonist of nicotinic acetylcholine receptor(nACHRs) in the hippocampus and has been implicated in learning and cognitive functioning
- Another mechanism of action of memantine is as an agonist of dopaminergic D2 receptors, which helps to enhance neurocognitive functioning
- Further research is required

Thanks


Executive Function
Information Processing
Sensory Processing
Verbal & Nonverbal Communication
Autism Spectrum Disorder
Repetitive Behaviors
Social Awareness
Motor Skills
Perseverative Thinking