Lecture 1:

- Neuroplasticity (theme) – adapt to env. Stim., compensatefor inj, age depend.
- Embryogenesis – zygotw → inner cell mass → embryo, (trophoblast → placenta around embryo), nervous system develops from **ectoderm germ layer** which forms neural tube and then brain
- **QUESTIONS**
- how is the brain dynamic? Changes in brain structure are critical for learning and memory

Lecture 2: Genetics

- human genome project correlates detected mutations and clinical symptoms
- whole genome sequencing identifies entire genome sequence of an organism at a singlw point in time
- rna sequencing detects presence and quantity of rna in a gneome. Effectively shpws expression of proteins
- critical periods: senses – infancy, language – btwn infancy/childhood, higher cog.- into adolescence.
- Env/gen work together to shape someone. Genes (nature) are enabled/activated by env. AKA genetic susceptibility AKA epigenetics. Env stimuli influences neuronal activity which then influences the expression of genes.
- Complex geno-phenotype relationship. Much variability in symptoms via expressivity (same mutation different output) and penetrance (how often does a mutation result in a disorder)
- canditate genes: gene suspected to be involved with a particular disease. Usually begins with family members with same disease. Use gene maapping to detect mutations. Localize gene to a chromosome. identify area of chromosome part of mutation and then look for specific SNP's in that area.
- Genetic disorders = chromosomal (parts of chromes mutated, aneuplody), monogenic (mutation in a single gene/mendellian), sex linked (x or y)
- many neuro duseaes or polygenic and multifactorial (mitochondrial disorders
- expressivity is severity, penetrence is if its present or visible (frequency of expression)

Lecture 3:Environment

- intraueterine infection aka zika, HSV, chlamydia. Zika = diverts resources away from mechanisms needed for neurogenesis. HSV = weakening of BBB, psych effects, transmission of virus to fetus which activates inflammatory mechanisms. Chlamydia = blindness (neuronalinfluence?) preterm birth,
- stress → cytokines which are inflammatory messengers. Reduces levels of BDNF and neurotrophins and increase toxic protein levels therefore stress = bad.\
- tetrodotoxin = Na channels botulinum toxin = inhibit AcCh release art neuromuscular junctions
- mercury is reactive with selenium which protects neurons from oxidative damage.
- Smoking correlates with decreased fetal head cirumference
- mental instability = NT imbalance = passed on to child/
- 4 dietary substances in neuronal dev. = folate-> spina bifida/problems with neural tube folding choline omeg 3 water

Lecture 4: diagnostics

- Ultrasound: brain and spinal chord structures (embryonic/ fetal development
- Nuchal translucency: fluid filled space in fetal neck. Measured on ultrasound btwn 11-13 weeks/ 3.5mm is elevated (bad). NT correlates with spont. Fetal loss, trisomy 21, heart defects/rare

genetic disorders.

- IPS Amniocentesis : aspire amniotic fluid containing fetal cells. Do karyotyping, PCR, FISH, PAPP 15-20 WEEKS
- IPS Chorionic villus sampling: collect fetal tissue and perform dna analysis look for chromo errors/errors in metab. 10-14 WEEKS
- Maternal serum proteins: a-fetoprotein (hi or low assoc. w/ neurodev. Iss) fetal blood sampling = high risk of fetal loss.
- Fetal testing is multimodal, longtitudal (imaging, molecular, genetic,psycological etc)
- major obstacles in neurodevelopment assesment – clinical assesment during development is diffuclt, psycological testing is hard because there are many developmental chnges during childhood,
- newborn assesments = alertness, sleep patterns, crying, excessive drooling, head shape
- developmental problems are hard to detect in infants due to limited language and motor ability
- important to evaluate learning and meory deficits early.
- fMRI+PET = functional - ultrasound+MRI+CT = structural

- Lecture 5: Cognition and learning disabilities
- DSM5 diagnostic and statistical manual of mentaldisorders. Assits in planning treatment strategies and symptomology
- Twin studies are strongest evidence towards LD, but also caveat towards environmental since its not 100percent.
- Genetic studies look to find a specific chromosome → locus → candidate gene etc. dyslexia has a link with chromosome 15 and also 6
- environment can cause"programming" effects via pruning and strengthening of neural connections.
- LD comorbid with other neurodevelopmental disorders (often two independent conditions that aremediated by common genetic factors + overapping risk factors Mg ions cause selenium degradation which can lead to exposed neurons which is a obviously a recioe for disease.)
- LD in adolescents typically carry on forwards into adulthoof and comorbid with depression, agression, social incompetence etc
- CNS root of learning disabilites. Cortical development is crucial
- Dyslexia is a dysfunction in cognition. Problems with phonetics and breaking apart words into syllabkes, rhyming etc. some part of language aqquisition is imparied. Sylvain fissure perhaps since it is near tempoeral and parietal cortex which recieves many auditory and visual cues. Problems here lead to misinterpretation etc
- reading is learned beha.
- Wernickes area = comprehension

Lecture 6 -FAS

- alcohol exposure in 1st trimester yields facial abnormalities and brain maldevelopment
- spectrum disorder
- syndrome = consistent pattern of multiple manifestations known to bave a specific cause
- FAS – alcohol crosses placental barrier- CNS defects, low birth h/weight, face.
- Craniofacial features of FAS = weight height small head. Underdevloped jaaw, small eyes, short "up" nose, flat face, thin upper lip, abnormal corpus collosum (axons). Corpous collosum should have thin black area. Sometimes its wide sometimes narrow in FAS. same can be seen in mice
- corpus callosum is most susceptible to distruption within 1st trimester (3-12 weeks) as well as many other structures

- predispostion to addicitve behavior, attention LD cognition defecits
- testing for FAS – ultrasound for structures, MRI, face features when born
- alcohol crosses BBB and induces cell death processes.
- Ethanol is a GABA agonist (stimulates) gaba receptor which yields a sedative effect on brain activity
- benzodiazeoines, barbiturates gaba alcohol all bind to gaba receptors
- gaba receptors cause chloride influx into neuron which causes a more negative charge, inhibiting neural activity.
- In rats... reduced: neurogensis in cortex and cerebellum, global reduction in neural formation, hippocampal mallformation
- reservatrol can promote neuroprotective effects

Lecture 7:80HD
practical/working definition
what is attention = an effortful process. What we have chosen to focus on.may or may not be motivated by something else. In adhd planning and execution an self regulation and sustained mental effort are all impaired.
dsm diagnostics
comorbitdy factkrs. Hyper activity and impulsivity
pharmotherapy

- **Characteristics of adhd**
- adhd= impaired planning/execution, self regulation, sustained focus/mental effort
- symptoms does not equal ADHD. Needs to have negative consequences/impairment
- inattentive adhd subtype = difficulty with repetivie effortful tasks, lethargic/hypoactive
- Inattention (problems remaining on a task/inability to inhib performing more interesting tasks
- impulsivity = thinking before acting, following rules, weighing conseqquences self control
- over arousal = lack of inhibition, excessively restless, emotionally aroused easily
- difficulty with gratification = require frequent predictable meaningful rewards. Difficulty with ong term goals. Negative reinforcement issues
- emotions/locus of control = rollercoaster of emotions in childhood,project blame onto others
- **possible causes**
- **neurobiology**
- abnormalities in basal ganglia (repetivie tasks) smaller prefrontal cortex (planning) and cerbellum (gratification + impulsivity)
- delay in cortical thickness during development, especially in pfc.
- Dopamine = reward/motivation, norepinephrine = emotional disregulation, serotonin = memory
- problems with DbetaHydroxylase is associated with adhd and attention (dopamine to norepinephrione. Less enzyme may lead to an excess of dop which makes impulsivity increase, and norepinephrine would be lesser and lead to emoit
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- mesolimbic dopamine system involves VTA Nac PFC. FMRi shows less/impaired signaling in reward pathway
- paradoxical effects of stimulant drug treatment for hyper activity:
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- **genetic/environmental risks**
- DAT1 = dopamine transporter gene, drd2 and 4 = receptor, mao-a, 5htt serotonin transporter

- manganese (in soy based infant formula) accumates in children.higher manganese levels in brain correlated with loss of dopamine. Also lead
- hypothyroidism, enceaphlitus, traumatic brain injury are predispositions]
- genetic predisposition leaves one vulnerable. “correct” environment conditions are more effective. Imporper development occurs. Snowballs, etc
- early symptoms can be transient therefore difficult to treat. May diminish in childhood or devlop into anti social behav, conduct disorders
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- **treatment**
- adhd is a multimodal treatment maintained, with medication over a long period of time
- methylphenidate, dextroamphetamine

lecture 8: aggression

- **types and characteristics**
- impaired cognition = unwarranted perception of danger
- impaired avoidance = high anxiety/impaired stress response
- impulsivity
- delayed neurodevelopment = altered mechanism for communicating emotions
- trauma
- impairment in emotional regulation = low threshold for anger
- proactive = goal oriented, aimed at a specific person or thing, probably planned
- reactive = reflexive aggression in response to percieved harm or violation, emotional outbursts
- aggression is characterisic of depression bipolar ptsd alzheimers dementia etc
- oppositional defiant disorder =
- conduct disorder = anti social behaviors
- **brain structures**
- temporal lobe = amygdala (reduced volume in p's with conduct disorder), hippocampus, superior gyrus = emotional memory response, fear,anxiety
- thalamus = filtering, processing, relaying info
- pfc = dorsolateral: planning motivation = orbitofrontal: inhibtion of impulsive aggression (increased in p's w/ conduct disorder = medial: response conflict
- anterior cingulate = decision making emotional processing
- hypothalamus = sexual drive
- ventromedial pfc = delay of gratification
- Nac = reward enforcement
- **neurobiology**
- serotnin active in orbitofrontal and cingulate cortex with impulsivity
- behavioral inhibition linked to four exec functions: working mem, self reg, internalization, reconstruction. Pfc processes much of this
- complex with multifactorial behaviors. Best treated by identyfying underlying problems (primary symptoms
- long term cortisol exposure interferes with serotonin metabolism
- 5 symptomatic domains = impulsivity, (thoughtless rapid aggr acts. affective instability, emotionally charged attacks. anxious/hyper arousal, outbursts of frustration. cognitive disorg, poorly organized confused acts. aggression behav. (predatory)
- childhood behaviors as predictors: diificult temperment, negative parenting

- serotonin plays a major role on impulsivity in orbitofrontal and cingulate cortex
- inhibition of mao during fetal brain development is a risk factor
- beuroendocrine nt systems involve testosterone and estrogen + serotonin and vasopressin. Raphe nuclei project to cerebellum and hypothalamus. Hypothalamus leads to basal ganglia then pfc
- testosterone may be a factor because aggression is more prevelant in males. Cortisol causes disregulation of stress response.long term exposure to cortisol suppresses serotonin metabolism in limbic system.
- Inverse relationship btwn 5ht and aggressive behav
- vasopressin linked to aggressive behavior in lateral septum. Testorterone interacts
- **treatment**
- stimulants to reduce impulsivity, antipsycotics, mood stabilizers