Schizophrenia:

Hallmarks: cognitive: dysfunction in executive tasks, attention deficit, working memory function deficit; positive sym: alluciinations, illusions, thought disorder; negativr: anhedonia, poverty of speech, social retreat.

Progression of symptoms: cognitive, social, working symptoms – anxiety and depressive symptoms – social retreat and subjective cognitive changes – prodromal symp – psychosis (in adulthood)

Schizophrenic brains have enlarged ventricle, smaller amyg and hippo and pfc. Also the cell polarity is not nicely defined (maybe some migratory problem).

NMDAR hypothesis: morphological changes to NMDAR structure leading to disturbed signalling or connectivity.

DA signalling hypothesis: it seems that an excess in D2 dopamine signalling leads to pos symp while a defeicti in D1 DA signalling to nega symp in the dopaminergic pathway.

Duncan model: scale: genetic predisposition vs environmental stressors: 1/x graph as threshold line for schizotypic symp.

ASD: hallmarks: social: do not form peer to peer relationshjips, hard to maintain conversation or intitate it, avoid eye to eye contact, obsess with one object, perform routines in an infinite loop like fashion (like rocking the head)

Comminucation: do not develop language or really late and only partially not always fully, do not respond immediately

Behavioural: no make believe or imitative play

Clear genetic evidence: concordance is 60% (in dizygotic twins it’s 3-10%)

Environmental stressors: mother took anti convulants during pregnancy, viral trauma (rubella or cytomegalovirus), thalidomide use.

ASD brain: no or almost no corpus callosum, smaller cerebellum, smaller pfc, loss of purkinje cells , changes to overall brain sturccure, smaller and more densely packed cells, less dendritic arbors, changes in synapse formation and elimination

Similar diseases: childhood integrative disorder, aspergers syndrome, PPD-NOS

Mental retardation: neurotrypsin first identified non-syndromic an not X-linked gene: protein that cleaves agrin which is a NMJ gene needed to make synaptic formation with muscle. In CNS, it also helps in new synapse formation. When neurotrypsin is not functional (nonsense mutation) then agrin does not work in CNS and there are not really new synapses: mental retardation as an underconnectivity syndrome.

LTP still works in exisiting synpses though, but not in new ones since they cannot be formed.

Syndromic form is obvious: it’s down syndrome (trisomy 21).

Fetal alcohol syndrome is related to mental retardation: it’s when mothers drink during pregnancy, problems in brain development: no CC, changed brain structure. Facial changes: smaller eyes, very thing upper lip, the long pit between nose and upper lip lacks for the most part.

ASD hallmarks:

Behavioural: occupied with one object for long times, sticks to nonfunctional routines or rituals, stereotypic repetitive motor mannerisms, only has one or few patterns of interest

Social: does not share happiness or joy sponateously with environment (e.g. the mother), avoids eye-to-eye gaze, does not develop peer-to-peer relationshiops, lack of emotional and social reciprocity (does not understand facial expressions)

Communication: not language develop or only partial and late onset (but can be full development), hard to maintain conversation or develop one, does not do make-believe or imitative play, usage of stereotypic and repetitive phrases

MNS: neurons that activate the temporal lobe and it is as if one did the task oneself when observing someone else actually doing it. Needed to understand intentions and interpret emotions

Cell migration: 4 types: somal translocation, glia guided locomotion, tangential migration and ventricle directed migration.

Somal translocation espeically in the beginning around E8.5: cells from VZ migrate to PP radially (pial surface directed).

Glia guided locomotion: glia cells extend their arms to the CP and above and neurons can use it as a rope to migrate to the CP basically (start in VZ). Around day E12. Especially, pyramidal cells.

Tangential migration: neural cells migrate from the ganglionic eminence to the marginal zone. From there they will migrate radially to the CP. Those are especially interneurons.

Ventricle directed migration: interneurons can also migrate tangentially to the VZ and then radially to the CP.

In the cerebellum, granule cells first migrate tangentially to the most other layer and then anti pially directed (they simply go inwards, instead of outwards like in the cerebral cortex). They form clearly distinct layer: at the most outer part beginning: oEGL, iEGL, molecular layer, purkinje cells layer, internal granule layer.

Purkinje cells migrate radially to the pial surface basically though.

Diseases and genes:

Stop signal malfunction: POMT, POMGnT1, fukutin – cobblestone lissencephaly

Initiation dysfunction: FLNA, argef2 – periventricular hetereotopia

Lamination migration defect: RELN: lissence, cerebellar hypoplasia

Ongoing migration defect: Lis1, dcx – lissence, subcortical band heteroptopia

Derivatives of NCC:

Cranial: melanocytes, sensory neurons, glia cells, bones and cartialage, connective tissue such as eye

Vagal: sensory neurons, glia ccells, melanocytes, smooth muscle cells for heart trunk, cardiac tissue, enteric neurons

Trunk: glia cells, seonsory neurons, melanocytes, autonomous neurons, chromaffin cells for adrenal medulla

Radial migration also involved reogragnization of the cytoskeleton: elongation of he expolriing site by elongating their tips through polymerization at the tip end (costs ATP) of actin filaments and insertion of microtubules also through polymerization. Then the nucleus has to move forward through nucleokinesis (with the help of microtubules and their associated motor proteins), and the rear side retracts. True for somal translocation and glia guided migration.

Also if not enough neurotrophins are around, then some cells will also undego apoptosis even if they found the righ area. Probably the case in very early innervation if at all, due to so many axons present at that tiem. Further pruning also occurs depending on activity and LTP so that weakly activsated synpases will be eliminated eventually – see Ca2+/arc signalling: climbing fibers on purkinje cells: When activated, there are specific receptors tha leak in Ca2+ which in turn activated Arc. Arc eliminates other synpases farther away from the activation site suhc that we have monosynaptic innervation at the end.

In initial final targeting finding, axons grow by elongating the top. Later, when contact has been finally established with the target, the stretch the rest of their body – obviously because the organism grows and becomes bigger, so they have to keep up or they will tear apart due to mechanical tension.