Notebook #5

Notes - Oxford Neur...
Summer 1938 + ...

Neuro-embryology Chicago 1938

Copco

COLLEGE

NOTE BOOK

Sperry, R.W.

Mon-Thurs.

{Babin Schaeffer - Am. Mus. Nat. Hist. - N.Y. City
{Shirley Hafe - Harvard Glass Flowers - Gray Mus.

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Detwiler's Neuroembryology (see bibliog. — 1936)

There are no nerve fibres not directly connected at some point w. a ganglion cell. ie grow out by cells

Chimera = composite animal formed by grafts

Dissecting scissors & glass needle & hair loop used operations micromanipulator rubber came into use. & vital dyes used

Vital dyes: Nile, blue sulphate, neutral red, Bismark braun

Sheath cells of Schwann arise from neural crests

Sympathetic cells come from crests also and not from cord.

Myelin forms about axis of sheath cells along the axone.

Early unmyelinated nerves nerve a bit to direct advancing myelin-emergent nerve cells & to furnish inner sheath cells

Long myelin segments may be formed by end-to-end coalescence of shorter segments w. obliteration of intervening node of Ranvier.

Growing tips of single nerve fibres show amoeboid activity.

Myelin sheath is not a part of sheath cell, but of axis cylinder.

Neurilemma is an organic part of sheath cell

outward — what about connections inward?

No specificity of a given motor neurone for any particular muscle fibre. Distribution of nerves not an intrinsic factor

Segmental nerves posterior to brachial plexus of normal limb will innervate a grafted limb bud 3 or 4 segments posterior to normal position, so limb bud exerts a directive influence on growing nerves. (but not a specific one?)

Brachial nerves will be attracted to limb bud grafted anteriorly in gill region — against considerable opposition. Anterior spinal nerves also grow in. — what attracts 'em higher metabol? narcosis? skin? would an eye attract them?

Anuran limb buds & side of head became innervated by facial nerve. Cranial nerves will innervate limb buds. V-VII & IX-X ganglions innervate + extrinsic eye muscle nerves.

No morphological specificity between nerves + their end organs. Hind limbs innervated anterior & normal position.

Hamburger - frogs, extirpated limbs-sacral region + plexus from opposite side turned over and innervated denervated limb.

Rogers - Hyperinnervation of an embryonic muscle is possible added grafts of accessory units of spinal cord.

When limbs on both sides innervated by same brachial or lumbo-sacral plexus - do the limbs coördinate alternately or together? Done on frog - could it be done on amblystoma ? of reciprocal innervation etc.

Spinal nerves will grow toward nasal placodes & eye placodes. Sensory nerves will connect to muscles directly + innervate them. T

Eye does not seem to attract spinal nerves. Yes, accdg Detwiler.

The outgrowth of the nerve fibre is: a mode of protoplasmic movement and not a mere progressive differentiation in situ. Embryonic frog neuroblasts were explanted into frog lymph outside body of embryo = tissue culture. / Harrison.

3 theories - factors directing nerve outgrowth.

1. Chemotropism - Cajal - Forssman
2. Electrical - Strasser - Kappers - Child diffes in bioelectric potentials neurobiotaxis - expt'l support.
3. Mechanical - His, Harrison

Outgrowing cell processes became oriented in the direction of lines of force of the galvanic field. Those toward anode diff'd from those toward cathode.

Outgrowth is perpendicular to a weak current thru a conductor in the culture.

Weiss - fibroblasts from chick embryos respond to intimate structure of fibrin clots in wh. cultivated. Stretched film of plasma on frame + lines of tension influenced direction of growth. suggests chemical + electrical may influence groundwork that wh. fibres grow, but they themselves, mechanically guided by groundwork. — but this for fibroblasts, not nerve fibres — nerve fibres grew in all directions.

But nerve fibres directed in a culture stroked longitudinally while clotting. - mechanical environment

Repeated electrical expts w. negative results and explains em on mechanical grounds alone.

Explains growth to limb buds or any rapid metabolic center in mechanical terms.

[But what about growing thru opposition anteriorly and crossing over from contralateral plexus]

Nerve fibres toward centers of accelerated growth - explains the tracts formed thru-out ems.

[If so, couldn't one make an artificial growth center by stimulation with electricity - heat etc & get nerves to grow where they shouldn't in normal animal — use cold blooded animals - or current thru localized portion of embryo.]

Behavior of autoplastic transplantations = limbs excised and grafted in diff't place on same embryo.

Homoplastic transplantions = limbs from diff't embryos These are made during tail-bud stage of development. Get coördinated function w. opposite limb only when the transplant supplied by some of brachial nerves.

* Rogers - when a supernumerary brachial region of cord is transplanted between the normal cord and the limb bud, the limb may acquire nerves from the graft only. - normal adaptive motions may continue for long period of a time. But if the graft is composed of the 4th 5th 6th trunk segments of the cord, & nerves grow into the limb, it's function is in no way adaptive - only slight twitches.

Peripheral mechanism = same in both cases, but central is different.

(What part of connections were made in these 2 cases between the graft and the CNS?)

Anterior limb rudiment 3rd - 5th somite centering on 4th.

Limbs innervated by 5, 6, 7, spinal nerves don't coordinate if 5th, wh. is only normal brachial, is cut. (do they if 6th? 7th?)

[But if you cut large nerve to any limb, it's apt to destroy the coordination]

Normal limbs.

3rd cut — shoulder function affected
4th " — forearm " "
5th " — hand " "

When have 2 limbs - one transplant and another in normal position - regenerated and supplied by 3rd & 4th nerves only - it coordinates OK.

In some cases a limb exhibits full function when supplied by only one segmental nerve.

Sometimes when only a few fibres of 5th nerve (+ 6th & 7th probably) supply grafted limb, it exhibits full function.

When have a regenerated limb 3 & 4
and a grafted limb 5, 6, 7 nerves both sets of mis
contract synchronously & w. same degree of intensity.

The brachial nerves may be heavily overloaded – no extra central cells, so it's the branching of the axones

Supernumerary limb is grafted next to an orthotopic normal by nicking cutting one or more of the nerves to the normal limb in making the wound for insertion of the supernumerary and then the nerves regenerate into both limbs and you get homologous response. The nerves regenerated at random.

Resonance theory of homologous mots – not resonator in physical sense

The CNS can emit diff't forms of excitations and the specific m. responds to those to which it is attuned.

The central coördination consists in combining the excitation for mis that are to function at a given moment.

All components of an excitation are conveyed to all m.s, but each responds only to its specific component.

Weiss - toad - implanted to fixed skeletal points & under tension various individual leg muscles from one side of body to the other & led into the implanted muscle a branch of the lumbo-sacral ~~com~~plexus. – became functional attached to recording device. Homologous mis fired synchronously.

Works no matter what nerve branch is introduced into grafted m. or what combination of mis is employed.

In earlier papers the end-plate emphasized as the selective apparatus. – Later the whole motor neuron i.e. gastrocnemius bid spread some substance or influence that would make the nerve gastrocnemius-selective.

Each m. modulates its nervous [illegible] entering a nerve fibre w. old periphery & connecting it with a new results in its losing the old module and acquiring a new.

but what about splitting of axons & 2 mods

C.n.s. = playground of integrated central activity.

Central sending system identified w. the neuropile.

If selectivity controls the admission of impulses from the neuropil to the modulated peripheral fibre, no trace of the unmodulated central activity can be expected to be found in the peripheral fibers nor in the modulated central fiber tracts which, in a sense, represent extensions of the periphery into the centers

The unsorted mess of excitations present in the neuropil then is picked over by motor cells & intercenter cells and sent on.

Just how much of the sorting-out occurs in the motor neurones & how much of it is already done by sensory S? How much does it reduce the amity of afferent excitation from centers

In order to coordinate the m. contractions have to be correlated w. the peripheral conditions.

Anter. limb rudiment grafted to head in place of ear vesicle shows extensive graft. o correlated w. jaw muscles still observable six years later.

Works w. a limb that has been functioning in its normal position in larval life for several months.

Hind limbs grafted close to lumbo sacral plexus work homologously only when supplied by [illegible] the shortest activity and occasion when jaw muscles are moving and all other mis of body musculature.

When supplied by nerves other than brachial or lumbo-sacral, limb reactions are typically assoc'd w. the mi's also supplied by these same nerves.

Limits of limbs grafted to head are usually much more extensive than those grafted to trunk region.

When end-organ or peripheral part of a neurone in adult organism is destroyed & does it regenerate, the ganglion cell atrophies. (life of ganglion cell depends on end organ) In embryo it fails to develop.

so maybe central growth depends on end-organ

Growth of nervous system in 2 periods:

1. 1st, growth & differentiation independent of function
2. Further " " dependent on function

Forelimb rudiments of amphibia, chicks, extirpated and marked deficiencies in peripheral nerves & sensory & motor nerve centers followed.

Neural placoded excised from amblystoma – forebrain mapped up to time when functional activity begins – later hypoplastic development.

Detwiler – excision of amblystoma forelimb accompanied cellular reduction 50± % in brachial ganglia.
A sensory hyperplasia in ganglion of 6 & 7 nerves where new limb is grafted.

When limb rudiments grafted to head, cranial ganglia likewise undergo hyperplastic development.

Grafts in tail bud stage make little difference up to time when function comes in 11-12 days after operation.

Grafting fully differentiated limbs in rana & metamorphic animals – forbidding fitting of the nerves – also results in hyperplasia in ganglia – but there cases limb connects w. only one spinal nerve. Ganglia are already well differentiated.

There seem to be indifferent cells in center of ganglia that grow & proliferate under expt'l conditions.
[Favors a chemical influence on growing neuroblast]
Overfeeding favors hyperplastic growth & underfeeding decreases hyperplastic growth.

In chick excision of limb buds results in retention of correctly ventral horns (motor). & maybe in amblystoma & anurans.

Detwiler - in amblystoma the no. of motor cells is unaffected by limb excision. (one or both forelimbs) The grey areas of spinal cord unaffected by removal of one limb, but a volume decrease of 13% in mid motor roots volume decrease of 32%

Conclude the number of motor cells unaffected, but the size is affected. Average area of plane thru motor neurone is reduced 8% for one limb excision and 20% when both excised.

Growth & function of one group of neurones may affect " " " of another related group.

Motor centers of cord fail to show hyperplastic as well as hypoplastic development.

Evidence against Detwiler saying frog spinal cord shows hyper & hypoplasia of motor cells.
Hamburger on chick shows hypoplasia of 61% motor cells when limbs excised in 68-72 hrs. stage.

Motor centers in cord respond to peripheral changes in chick & amuran but not in urodeles. The two former have a ventral horn of grey matter, but the latter doesn't.

In Amblystoma the motor neurones are located in the center of the spinal cord & not separated from correlation apparatus. They figure that groups of

neurons which have migrated away fr center of sp cord (spinal ganglia, anter, & poster horns, if present,) equiv under control of peripheral fields. But 40% of cells of anter horn in thick are developed independently of peripheral field.

Coghill - behavior pattern develops w. growth of nervous system & its parts & from massive to discrete.

* In amblystoma neural tube stage - when 3,4,5 segments of nerve cord replaced by 7,8,9 the animal develops & acts normally. In later stages abnormally.

7,8,9 segments showed hyperplasia

345 replaced by 7,8,9 & limb excised, but the hyperplasia was there just as before.

345 reversed and activity normal & OK. Thus no inherent predisposition on part of a given brachial nerve for its normal musculature. 5th hyperid & 3 hypo'd.

[Do such rats as animals that have definite inbuilt reflexes, see how early they're built in.]

The conditions determining development w in cord determined not by peripheral, but central cord factors in Amblystoma. Higher up scale, periphery counts more.

When 1,2,3 put in position 4,5,6 they don't show hypoplasia.

Support Coghill's notion that certain local regions of cno undergo differentiation & proliferation from hereditary causes.

When medulla is substituted for brachial region, there is no effect on segments cephalad & caudad to graft. Thus there's a difference between med. & anter. part of cord.

Certain regions like 1st & 2nd segments possess almost fixed inherent capacities for cell proliferation whereas other regions are more labile and respond by increases or decreases in accordance w. the position they occupy in the central axis.

Anterior segments grafted caudad never reduced to anterior the caudal position normally has & sometimes proliferates more than if left in anterior.

Most of increase was in sensory areas wh. retain embryonic character longer than ventral.

The inherent proliferative capacities are higher at anterior end of cord than at more caudal.

Mere injury (5-25 days) doesn't produce cell increase.

It seems that fibers arising in medulla and invading cord have a stimulating effect upon cellular proliferation When medulla cut off and separated by limb rudiment or pronephros, there's hypoplasia in caudal segments & those present are those wh. arise w/out interaction of bulbo-spinal fibers.

When lumbo-sacral region is isolated, same thing happens

when units of cord transplanted outside normal cord & outside myotomes there is extreme hyperplasia.

Cellular proliferation & differentiation go on w/in cord and brain before projection fibres laid down. Later on growth affected by fibres.

When units of cord transplanted inside myotome, they are smaller than normal ~~hypoplasia~~ = size reduction.

The ingrowth of olfactory nerve stimulates growth of the olfactory lobe in telencephalon.

Burr grafted olfact. placode + telencephalon caudad to anterior limb — in one case left exposed to surface so function, in other case buried — both developed the same — so function not involved in development here — [but question as to whether graft actually functioned]

Transplant supernumerary nasal placode — two fuse w. extra fibers and ingrowth causes hyperplasia in olfactory lobe.

Sometimes grafted olf. nerve wandered back to enter diencephalon & caused hyperplasia there in thalamic tracts, or to opthalmic division of 5th & " in opthalmic ganglion.

When Tigrinum substituted for Punctatum placode, get hyperplasia also.

Burr finds rhythms of proliferation in nervous system corresponding to ingrowth of sensory fibers. Deduces that olf. n. enters brain where it does because of center of active proliferation at that point, & not vice versa.

Lot of evidence that local regions of accelerated proliferation influence ingrowth of growing nerve roots & also that entrance of nerve itself into the neural wall stimulates cells in that region to increased activity thus relation = reciprocal.

Burr says attraction due to bioelectric effects of increased metabolism.

* Optic cups grafted to position of otic vesicle develop an optic nerve wh. enters medulla IX-X gang complex & V+VII. All of these centers underwent hyperplastic developt.

Normal & supernumerary eyes fuse & produce hyperplasia.

Coghill points out that nerves grow while they function.

But anesthetized tadpoles supposed to be evidence that coordinated patterns can be grown in w/out excitation of neurones.

Harrison grafted pigmented anterior half frog to clear posterior of another frog & saw pigmented cells move back to form lateral line sense organs.

Tigrinum limb on punctatum grows larger than normal
Punctatum " tigrinum " smaller " " .
Similar for eye, ear, & gills.

Feeding experiments seemed to indicate it was the "nutrient level" of the two organisms wh. made the diffce.

Tendency for graft to maintain growth rate independently host, but beds where host factors will modify this rate even under conditions of "maximal feeding"

When spinal cord grafted, it accommodates itself very early to dimensions of host.

When tigrinum brachial region grafted, it regulates to host size punctatum
limb development & function were normal.

[How far could this be carried w. different species?]

Maximal feeding alters at 1st, but in end comes out same

The segmentation of the spinal cord and peripheral nerves in urodeles is entirely subservient to mesodermic segmentation and intrinsic segmentation is non-existent.

Segmentation of ganglia suppressed by absence of somites in a deficit region & abdominal somites → aberrant ganglia

It is presence of medial surface of somites that brings about differentiation and segmentation of the ganglia. Lateral surface lacks formative quality.
A mediolateral gradient in the somites.

A formative role is ascribed also to cartilage.
Detwiler has evidence vs. above of Romanes, but he used older embryos.

In all classes of vertebrates, the limb musculature arises from unsegmented mesoderm.

Cranial nerves are able to grow and reach the developing limb rudiment without any mechanical guidance by the corresponding myotomes. tho the segmental character of ganglia & nerves to limb is influenced by the myotomes in brachial region.

When 4 somites substituted for 3 in brachial region, get 4 ganglia developed instead of 3 and limb functions O.K.

[What about these primitive simple coördinations being inbuilt then? Doesn't look as tho it were so much a matter of inbuilt connections as of types of discharges.]

When 5 substd for 3 didn't get extra ganglia, but got 2 extra nerves to the limb.

Grafting unsegmented mesoderm from caudal region of younger embryo & 2 extra arches and ganglia developed, so 5 instead of 3 to the limb.

When crest cells cut, ganglia develop anyway.

In lower vertebrates, the maximum extent of the limb rudiment determines the no. of spinal nerves to form the limb plexus. The no. corresponds to the given no. of myotomal segments when the initial nerve connection is made. But moving limb rudiment caudal several segments does not result in corresponding shift of plexus.

In higher vertebrates where limb muscles no longer derived from muscle buds, the ingrowth of the corresponding segmental nerves appears to be occasioned by an attraction on the part of the developing musculature at a time when it occupies its greatest relative extent in the embryo.

Write out the main problems points in conditioning so will have 'em always in mind while studying neurology & many find answers to problems.

Mauthner's fibres = 2 giant neurones, of gigantic size and of high differentiation lying in medulla, lateral position at level of entrance of VIII nerve. Found in fishes & amphibians, extensive dendritic connections.

Axones after decussating course caudally thru spinal cord in a ventral position where connections are made w. both motor & intercalary cells.

Each cell has 2 giant dendrites (lateral & ventral) and numerous small ones.

Lateral branches among VIII root fibers & cells of Deiter's nucleus.

Synapses must be located along dendrites as well as around perikaryon.

In amblystoma dendrite spreads along distribution area of all lateral line roots.

Makes a short path between acusticolateral centers and the motor nuclei of the m.s used in swimming. Makes a 3-neurone reflex arc.

Animals w. one ear vesicle removed show torsion in swimming. Fatigue more quickly than normal.

One Mauthner's cell removed — equil. OK but became exhausted quickly.

Both Mauthner's cells removed – equil. OK and exhausted about the same as removal of one neurone.

Both ears removed – postural tonus abol. no coördination of swimming strokes. exhausted quickly.

large axons conduct more rapidly than small ones.

Coghill finds M's fibers axons connect w. both motor cells and intercalated cells. So he says impulses passing caudad would inhibit local sensory-motor responses in favor of ~~all trials~~ total action pattern & at same time inhibit opponent on one side in favor of agonist on other.

* In cases where a single nerve fiber (supposedly supplies non-homologous muscles, the homologous movements are like-wise synchronized. (Resonance)

[Explain resonance in terms chronaxy?]

[Grow few nerve fibers w. sensory cells attached in nitro (tissue culture) & see if $ makes diff. in growth, synaptic connections.]

End bulb = bouton.

Boutons not demonstrable in kittens until post-natal stage of about 1 month

Reflexes are present before end-bulbs demonstrated.

Two types of end-bulbs: definitive (terminal) & collateral (boutons en passant)

Boutons en passant = less frequent than terminal

Both less common in medulla & lumbar region than in cervical.

Some ganglion cells have many around 'em, & some right close to 'em don't have any.

Boutons end on dendrites frequently as well as close to cell body & some seemed to find rest neither cell or dendrite

A few of large end-bulbs in cat showed a somewhat flattened edge lying against ganglion cells.

J. Comp. Neurology – Dec 15 1937

Dane Bodian – Dept. Anatomy, Univ. Chicago.

On perikaryon of Mauthner's cell in goldfish there terminate many large end-feet, innumerable small endfeet, a few small myelinated clubs, & many unmyelinated clubs.

Axon cap = muff around axon of M's cell & many of latter & types end on it. = unique type of synaptic apparatus.

100 or more large endfeet on entire perikaryon

100 to 150 " " on proximal half of lateral dendrite

many small " farther out on dendrite.

Axon cap = synaptic apparatus consists of collaterals of neighboring nerve fibers, small dendrites from the underlying cell body, & glial elements. Its central core consist of a network of unmyelinated fibers = continuations of axons from fasciculus longitudinalis medialis. They terminate

in tiny endfeet about axone cap, dendrites, & cell itself.
Tiny endfeet on distal portion of lateral dendrite and large endfeet on proximal.

Almost the entire surface of M's cell is covered wit. axon terminals of at least four distinct types varying in size from about ½ μ to 7 μ = (1,000th of a m.m.)
These terminals are circumscribed by a plasma membrane and arise from myelinated and unmyelinated nerve fibers.
No fusion, & they end discretely.
Interface membranes of contacted synaptic surfaces.

Herrick – Dept. of Anatomy Chicago

Amblystoma can still swim if brain above ear vesicles is transected off. Spinal cord and medulla oblongata including M's cells & ear vesicles.

Says in cerebral motor peduncle in connection with swimming adjustments & swimming movements influenced by the cerebral motor apparatus – the influence, if any, being autonomous of intrinsic origin ie central excitations due to metabolic or other internal events excite so called spontaneous activity.

The cerebral motor field attains a high grade of histological differentiation ~~before~~ with extensive fibrous connections w. lower motor centers before it is entered by nerve fibers from any sensory field – [what about proprioceptive fibers etc. from below]
[The means of olfactory and ocular perfn.]

Paul Weiss - Un. Chic. Zo dept. 1936

Has outfit for moving pictures. Grants from Rockefeller Foundation.

Now using large-sized & fast growing axolotl Ambly. mexicanum.

Expts done on free-swiming larva - several mos. old.

Sometimes use chloretone anesthesia but usually clamp down in web straight-jacket on operating table.

Autoplastic transplantation & on same animal.

Heteroplastic " use A. punctatum as donor & A. mexicanum as host.

Limb is excised w. good-sized disc of cartilaginous shoulder girdle.

Access to nerve plexus easiest at posterior edge of shoulder blade dorsal to base of normal arm.

A hole torn in skin and subjacent muscles separated bluntly to form gap bit smaller than base of transplant.

Nerve plexus located in depth of gap and the particular nerve wanted, is lifted & severed. A short piece of peripheral stump removed to prevent reunion.

The tissues close in on graft & hold it firmly. Can then twist limb into any desired orientation.

Some times normal arm limbs can be looped back from elbow region & inserted into transplant.

Some cases blood circulation is perfect and distal parts may become gangrenous & drop off, but they regenerate later. Of the same ages, there is better regeneration.

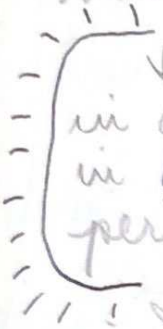
Regeneration of urodele limbs depends quantitatively on the presence of intact nerves at level of amputation.

Transplant limb = T, original = O.

* O continues to function normally - the loss of nerves deflected to T seemed not to impair its motility markedly [How come?]

T displays at any instant same type of mvmt as O regardless of its orientation. More accurately, the same homologous m's contract at same time.

The order in wh. m's of T come into function seems variable according to time receive innervation.



In toads there is a period when T muscles contract in general unspecific manner before they contract in specific homologous fashion. Of any such period in A's it is very short.

Intensity measured in terms of angles between joints of 2 different limbs O+T were equal. = "syndynamic"

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A rt. limb transplanted near lft. normal moves in mirror image of O — thus homologous response. If both limbs reversed animals walk backwards.

The homologous response is permanent and non-adaptable

When small limbs transplanted beside those of larger parts, the two show same angular mvmt.s $A_T \neq k A_O$

Homologous response fails when limbs transplanted between newt and salamanders (diff't genera)

∴ Homologous m's of diff't species more closely related in n's & chs than 2 / more homologous of same species

Myotatic reflex = due to passive stretching

Not due to specific connections because when a m. in T is stretched, both that m. & the homologous m. in O beside it respond by contraction.

These myotatic reflexes found mainly in m.s of lower arm.

They can be graded, the stronger the stretch, the stronger the reflex contraction.

Myotatic reflexes occur only in limbs that have a bit of tonus in'em at start. (Not fully relaxed.)

With 2 Ts all 3 give reflex response to stretch of one m.

One T had only forearm + hand inserted in body wall + it gave myotatic reflex of wrist and finger joints.

No myotatic reflex when animal is pithed.

Sometimes use faradic s to get m.o in tone for stretching.

When brain, including anterior part of medulla is removed, still get homologous resp. in myotatic reflexes. Fits in w. non-adaptibility of the response (higher centers for adaptibility.)

Cord sliced off gradually backward. When 3rd & 4th spinal segment reached tonus in O dropped but T innervated by 5th still functional.

Mosaic character of reappearance of function in transplants

Three possible relations between CNS and muscles.

1. Linkage may be due to selectivity in establishment of connections between regenerating nerve & m.
2. Linkage may be achieved under guidance of sensory discharges reaching the centers from the muscles of the transplants. (From myotatic misdirect)
3. Linkage may be physiological relationship between centers & CNS = "resonance principle."

1. Sometimes transplants didn't function because weren't completely innervated - may correct nerve fibers missing in that trunk. — + O functioned OK after one of its three nerves had been severed as maybe each nerve has fibers for all m's.

See Weiss & Rush - Supernumerary fingers in man 1936
Proc. Soc. Exp. Biol & Med. vol 34, p 569.

Weiss is tracing peripheral nerve connections by electrical stimulation.

The severed 5th nerve didn't have to be placed in T, it grew into it, if T placed close to cut end.

For electrical testing - animal (not always) decerebrated, anaesthetized pinned to board submerged in physiological saline solution. The nerves cut at emergence from spine & freed from adherent connect. tissue & blood vessels.

Then electrical S applied at various points in plexus.

Used induction coil by. 2 volts in primary circuit & electrodes of fine platinum wire less 1mm apart.

Stimulation done in air about liquid & excess water blotted off nerves.

Fibers counted by staining myelin rings, then filling in rings w. dots on paper - encircling groups of ten.

Concludes again that Ts have failed to induce the centers to send out fibers at an increased rate.

And that they divide so that at periphery T has as many nerve fibers as O.

Number of fibers in T varies pretty directly w. size of T.

Nerves follows old degenerated path pretty closely.

" in T are about same size as in O.

In order to produce normal number of fibers in T, the 5th nerve trunk must branch 6 times as extensively as normally.

The branching all seems to be done right at stump of old 5th nerve. Thus the branching takes place even before nerve enters limb.

(Nerve branch from cut surface & then don't divide any more till enter the muscles.)

3.4.5 nerves converge into plexus wh. is variable but fairly constantly it breaks up into 2 nerves going into limb – superior & inferior brachial. Both nerves become subdivided into 2 parts.

In axolotls 3 spinal gives more to inferior brachial
4 " " superior "

(Weiss's students are using histological techniques more & more)

By degeneration decide 5th nerve has share in innervation of proximal m's as well as distal. (all of fin. p. 501.

Forelimb of urodele has about 40 m.s.

For selective regeneration need about 40 types of nerves. and since nerves follow old routes without any apparent crossing or recrossing to reach specific m's in the limb it must be that the selection occurs at the root stump where the axones divide before regenerating into ~~the~~ T.

There are about 240 possible motor fibers going out to the 40 m's leaving about 6 fibers average per each m. By branching maybe get 15 fibers per m.

* Sometimes thinks he has case where a nerve supplying a particular group of m's regenerated so supplies an entirely new non-homologous set of m's! (But his evidence not very good here – should be done experimentally & this alone in mind.)

(Claims its incontestable evidence — but —)

Electrical stimulation of a cutaneous nerve leads to flexion in T and extension in O. ∴ same nerve fibers supplying non-homologous m.s.

The proximal portions of nerves in Ts were plucked out. Regeneration in 62 days as of 30 days where the degenerating nerves left in Ts. Degenerating nerve forms favorable substrate for regeneration of nerves — much faster than in other tissues.

Homologous response again O.K.

Regenerated along regular brachial & inferior brachial pathways despite absence of old nerve. But instead of 2 main trunks many smaller ones.

Assumes inferior & superior brachial nerves supply localized groups of m.s.

Nerve fibers formerly connected with only a restricted group of m's assume the task of innervating functionally the whole set of m/s. present in transplant.

An inferior brachial splits up into inferior and superior and grows out unspecifically. p 375

* Unmistakable axon reflexes were obtained in two cases. All central connections were cut, S of peripheral nerve in one limb caused response of one of several muscles in other". The reaction due to spread centred to point of bifurcation of the axone & then peripheral over the other branch of same axone into the other limb.

The two branches terminated in non-synonymous m.s in the two limbs.

The specificity of proprioceptive excitations has been demonstrated – (presumably a physiol. not genetic one)

Complete deafferentation of the left fore limb without damage to the motor innervation and transplanting them into vicinity of this limb a supernumerary forelimb to be supplied by one of the purely motor nerves of the plexus.

[Have to test for mystatic & other reflexes to be sure of complete deafferentation.]

Using dissecting mic the ganglia severed from their distal nerves & pulled out 2nd & 5th ganglia inclusive were pulled out. — Mortality about 50%.

Deafferentation (as in toad) failed to entail an essential impairment of the locomotor function of the limbs.

Pinching squeezing touching of deafferented limbs failed to yield any response in animals.

But in time 9-11 weeks - 4 weeks after function appears there regeneration of sensory nerves & sensitivity.

Homologous response as good as ever.

[Have to deafferent both sides of cord — the afferent impulses from one side may be enough to [illegible] central motor impulses of both sides. Try double deafferentation and decerebration to see how much of control is central & how much of it is peripheral. Mystatic reflexes also.]

Coghill – Wistar Inst. Anatomy & Biology

* Use myotatic reflexes and action currents.

Take O & T side by side – make myotatic reflex in O and see if corresponding m. in T contracts when T is differentiated and put in a posture that given m. in T wouldn't ordinarily contract in.

Bartelmez & Hoerr – Hull Lab of Anat'y Chicago
on Vestibular club endings in Amblystoma – morph. of synapse.
B&H = students of Herrick

Amblystoma = bull-head – on club endings of root fibers of VIII nerve on lateral dendrite of M's cell in Am.

Gray matter of living animal has consistency of thick porridge & it's not surprising that minute protoplasmic processes like dendrites & end feet should adhere together for cohesive forces must be great.

Cytoplasm & nucleoplasm of nerve cells = rather firm gels, under microdissection conditions – so probably already coagulated since all other cell media are fluid in living state.

Grey matter has exceedingly rich blood supply and high metabolic rate.

Coelenterate n.s. show synapses in living preparations stained w. methylene blue Leuco-base. Stained neurofibrillae. But evidence for such in vert. living n.s. is still to be established.

(R.R. Bensley developed cytological technique for glands.)

Method

Perfusion: fixing fluid injected into vascular system of living animal. Brain quickly removed and immersed in chilled fixative.

mordanting: After 12-24 hours put brain in Muller's fluid or 3% $K_2Cr_2O_7$ or $CuSO_4$ for 1-4 weeks. Wash w. distilled H_2O, dehydrate thoroughly and double embed in methyl benzoate-celloidin & paraffin

or use Bensley mitochondrial technique

No evidence of neurofibrillar continuity.

Go thru Histology text on n.s. Then find out about histological technique for n.s.

Evidence that each of elements of synapse has a limiting membrane, tho at contact only one membrane can be resolved.

[How do neurohumors flow, are not thru the membranes?]

Certainly lot of learned R. due to shift in posture & not change of neural tissue — how much of new R due to traces?

How explain contractions of limbs transplanted to head region on Resonance theory?
Contradicts the theory perfectly.

Nicholas - Zoology lab - Yale -

limb m. supply normal when arterial supply normal and aberrant when arterial pattern deficient. The greater the no. of n. fibers the more independent they are of the arterial pattern.

(*) vs Weiss. The m. contractions occur according to their location w. the musculature in association w. them. — the flank, the dorsal midline, the eye region.

Eye substituted Ts are integrated w. eye of opposite side or w. jaw muscles — tipping dish causes eye orientation.

Mouth sometimes occurs when rest of animal is quiescent.

Do limbs show coordination w/in muscles when placed in these odd positions? — if so peripheral posture central?

(*) When n.s. injured or when limb used to block the regeneration of severed parts of the n. syst. fiber cables pass from severed ~~ends to end~~ ends of n. cord into limb and cause responses which are similar to those normally secured over n. trunks, spinal or cranial. (not plexal).

* Coordination of limb mis w. the eye mis of the opposite side can be secured in exceptionally favorable cases, and in such cases non-homologous muscle groups function in well-defined correlation w. the displaced nerve supply.

Blake & Gerard - Dept Physiol. Chicago 1937

10/sec rhythm of restful waking state disappears in sleep.

Cu or Ag disc electrode placed on occiput & forehead + electrode jelly.

Under hypnosis 10/sec remains — abolished by suggesting a light was shining in his eyes.

A striking slow rhythm in deep sleep. ½ to 3/sec.

Kleitman, Mullin, Cooperman Dept. Physio Chicago

Weiss: in Collecting Net 1938 July v. XIII no 2. pp 29-32

Old ideas - connections

transplant gastrocnemius of toad to back & provide it with a strange limb nerve (from antagonistic muscle) it contracts according name.

Specific constitutional property of a muscle may lie in a specific bio-chemical differential.

* The muscles specify their motor nerves turning 'em gradually into selective receivers for central impulses which are of form adequate for this kind of muscle.

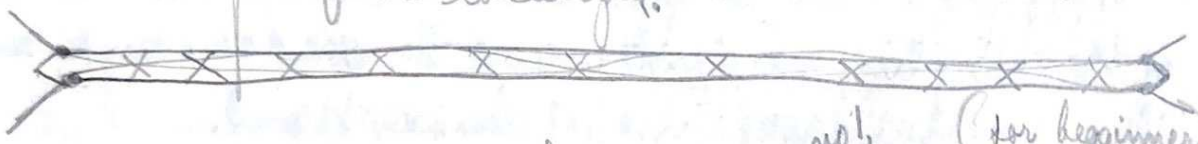
A severed from muscle & reconnected to new acquires new muscle specificity. This takes longer in older animals. (Why that growth in centers?)

Resemblances between mus-nerv specification and antigen-antibody correspondence suggested.

Central states – electrical, chemical ? There are as many different specific forms or modes of activity as there are individual muscles in the district.

Each half of spinal cord contains the center for its corresponding periphery. Either half can deal w. other side except by using discharge mechanism of other side as intermediary. (?)

Actions of centers localized.



(for beginner)

Gasser-1921- Am. J. Physiol. LVII, no 1, Aug.

Van der Bijl – The Thermionic Vacuum Tube
1920, 145 Chapter on Amplifiers.

separate batteries for each tube to reduce adventitia vibrations.

input connected to grid circuit directly or thru a transformer. in 1st instance grid circuit is shunted w. a R of 2,000,000 ohms, in latter w. 100,000 ohms

transformer has 4 taps permitting one to vary w switch S, the input impedance of the circuit to an optimum.

ea tube operated w. separate plate battery of 150/160 of no. 734 Eveready batteries of 6 volts each.

2 Rs of 500,000 ohms each were inserted between 2nd + 3rd grids and ground – wh maintain grids – to the filaments because of the potential drop in the filament Rs of the filament circuits.

In plate circuit of each tube is inserted a R of 500,000 ohms separately shielded. 2nd & 3rd grids are protected from potentials of preceding plates by the insertion of condensers fed w. a capacity of 2 microfarads their R = 1,000,000 ohms

tube & plate battery act as a generator of AC potential because of variations in the tube resistance.

This potential is applied across the circuit consisting of the coupling condenser and the 500,000 ohm R. and thus varies the potential of the next grid.

The AC output of the last tube is shunted across 500,000 ohm R thru a 1/4 microfarad condenser and the galvanometer string. Condenser has R of 500,000 ohms

Sometimes 3/4 microfarad condenser used. As alternative it's possible by switches S_6 & S_7 to connect output of last tube to the primary & the string to 2ndary of a transformer.

Optimum output impedance of this transformer is 500 ohms & input impedance matches that of tube.

Vac. tubes = Western Electric type V. designed for use w. a filament current of 1.3 amp.s, a grid voltage of -15, a normal plate voltage of 100, and a max. input voltage of 2.

Value of amplif. constant μ is 28. Plate current under conditions of our circuit is .45 milliamps.

The d.c. plate-filament R is ∴ 155,000 ohms & the a.c. R = 77,500 ohms.

Whole is in shield = wooden box w. top & bottom of ⅛ in steel & lining around sides of 1/16 in lead.

Box padded inside w. ¾ in wool felt.

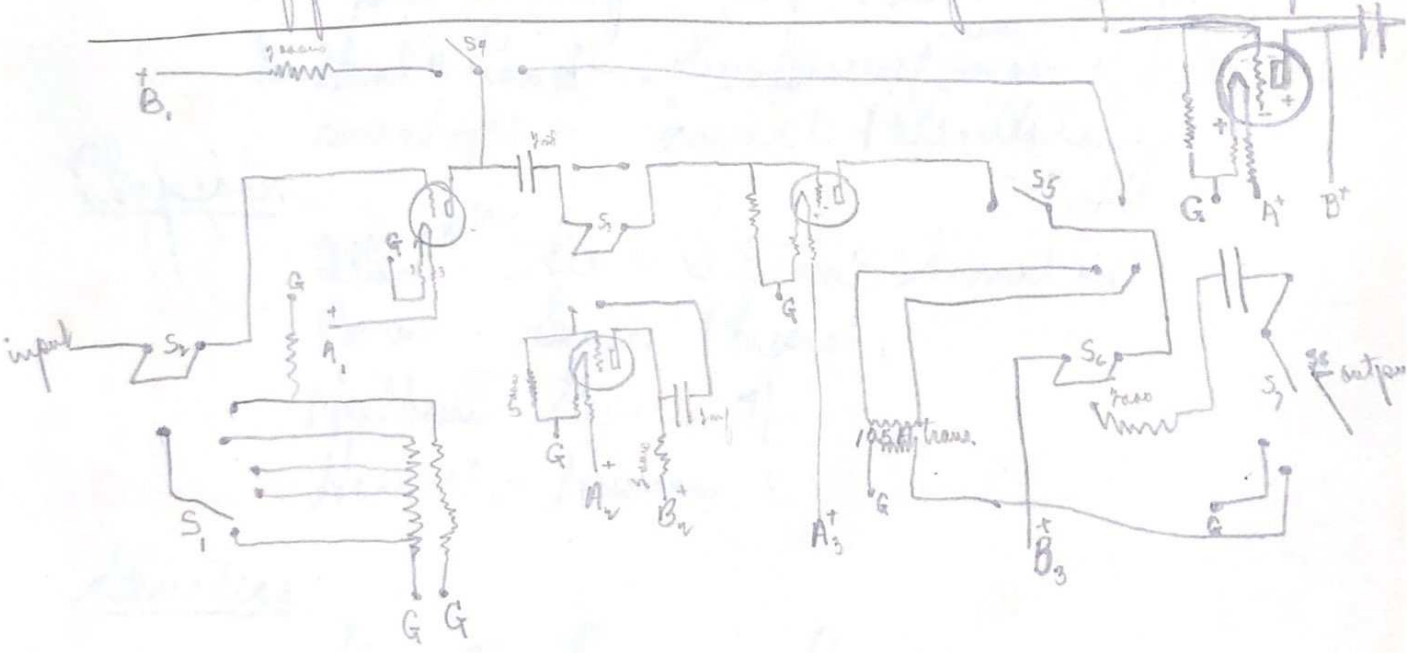
3 tubes screwed to pine board and the latter wedged about w. rubber bath sponges.

Switch S_3 cuts out one tube to give 2-stage amplif. using 2 outside tubes — they used only 2 tubes!!

S_4 & S_5 make possible to use 1 tube only.

whole box w. hinged lid & outside coaxing switches for batteries is supported on a rubber ~~sponges~~ & placed inside a galvanized iron box.

Been better to place tubes in separ. steel compartments w. ruffle round to make wiring shorter & simpler.



A lot more in article about amplifiers - curves. Pics of nerve arrangement in room etc. etc.

Used it for AC's from phrenic nerve of dogs.

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Embr

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Huxley + DeBeer - Exptl Embryology

" - Elements of " "

Needham - Chem Embryol - as reference

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McEwen - General stuff - grad

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Cyt in Anat.

Romer - Vertebrate Paleontology

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Kingsley - Cyt in Anatomy

Gregory - Orig. Face fr. Fish to Man (pop., but)

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Allen editor - Sex + Internal Secretion

Barnes - Gener. Physiol.

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Genetics.

Sinnott + Dunn - Genetics

Snyder - Heredity Blood groups

* Dobzhansky - Genetics + Origin of Species

Genetics cont.)

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+Biophysics + Biochem.

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advanced — genetic, cyto — Plenty of xing overs.

beginning — Darlington - Cytology (Recent advances in
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Am. Jour. Physiol. vol. 104 1934

Davis – Amply. str. galvan. & photo. camera for nerve act. c's
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Neuro-embr.

Growing limb influences course of outgrowing nerves. Is influence specific or general? Would an eye, a tail, etc. influence limb buds in same way?

— Spinal nerves will grow toward neural placodes & eye placodes.

Dong An Lab - Writ'g Electroencephal. Arch. of Neur. & Psych. v. 34 1935

Most brain waves below 30 cycles/sec.

used Boehme type 2-A undulators from Mr. J. W. Milnor of West. Union Telegraph Co.

"undulator" moving magnetic element wh. operates a small silver diphalt writ'g on moving paper.

good up to 40 cycles/sec. — & minimizes 60 cycle & m. AC.

requires an unusually large amt of power for operation

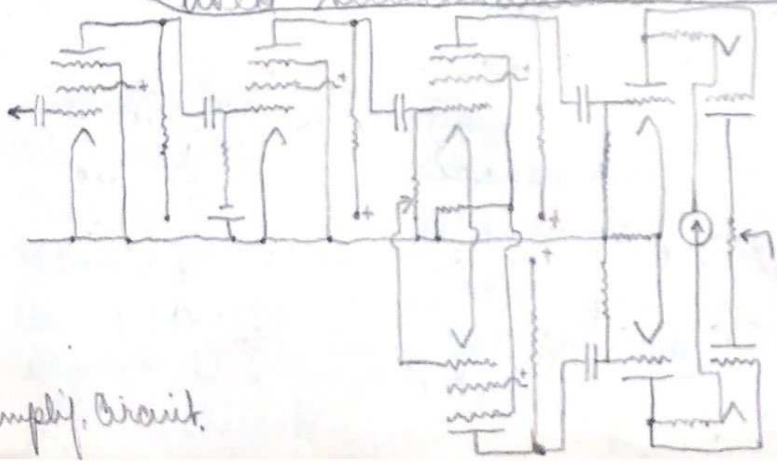
— a portable amplif. of 2 units

1st unit is operated by a battery & consists of 3 stages of resistance-capacity-coupled high-μ pentodes w. the last stage in push-pull.

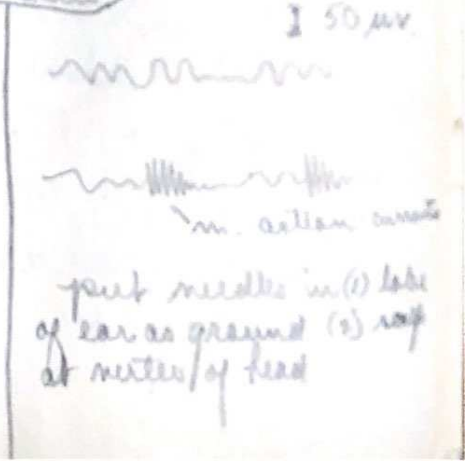
objection is that when condensers & grid leaks are made large enough to pass low frequencies, some annoyance is caused by the blocking of the amplifier when large contact potentials are applied to the input.

Continued using condensers large as 4 microfarads w. 1 megohm leaks. allows use of common B but 4 A batteries

used subcutaneous needle electrodes



Ampl'f. Circuit.



pair needles in (1) base of ear as ground (2) scalp at vertex of head

Harcum & Farbes – A Direct Coupled Amplif. for Ac.C's
Rev. Scient. Instrument. 5: 10 1934

* " " Davis — An Amp., Record. Syst., & stimul. devices
for the Study of Cerebral Act. Currents.
Am. Journ. Physiol. 107: 305, 1934

Adrian & Matthews — Brain - 57: 355 1934

Output unit operated on the 110 volt, 60 cycle mains. Amplif = a 4 tube modification of the Wold & Wynn Williams vacuum tube bridges.

The grids of 2 tubes in push pull are excited 180° degrees out of phase by the output of the push pull 3rd amplif. stage.

The other 2 arms of bridge are also vacuum tubes of the same type (2A3). they are connected that when bridge thrown out of balance by a signal appearing on input grids and in consequence a crap current appears in the leads, (in this case the undulator magnet) this current passes thru the cathode drop resistors of the second pair of tubes and unbalances these arms of the bridge.

This bridge connection is a completely efficient way of inserting a load into plate circuit of an amplifier and of balancing out the direct current component of the plate current.

An exceptly long linear characteristic can be obtained w/out excessive plate voltages. The small potentiometer between the plates of the 3rd and 4th tubes may be used to balance out the direct current components accurately. Need separate filament transformers for the 3rd and 4th tubes. — readily portable

Davis - Rev. Sci. Instrs., 1931, vol 2.

↓ String galv. too slow to give true picture of time relations in n.c. Nerve a.c. lasts about 1 millisec. (10)⁻³ sec. galv. take 3-4 σ String galv. takes 10 times as long to reach max. as a.c. it is attempting to record. ∴ acts ballistically.

Intrs. of cathode ray oscill. for a.c. by Gasser & Erlanger 1922 revolutionized nerve physiology. This depending on deflection of stream of electrons, has practically no lag.

But its sensitivity is so far below that of the string galvan. that depends on powerful electron tube amplifier.

3 stages beam coupled, capacity of these tubes introduces lag of about .02 σ = negligible.

This apparatus is complex and it is difficult to get record of single response.

Also pattern depends on discharge of a condenser as it's logarithmic curve & must be redrawn to get absolute picture. Gasser gets rectangular coördinates by placing vacuum tube in series w. timing condenser

Their contribution = shortening of the string of string galvan. Gilded quartz is used could get it thinner, less density, than tungsten (with. can be pulled lighter).

Light string follows better than slack but need more amplific. Very fine strings pulled by melting quartz rods, then gilded = delicate technique.

Matthews Journ. Physical 65. 225 1928 on amplifiers

Amplif. from Bell Tel. Lab.s informed 'em wanted to record a transient current, reaching max. in .3 o, input R 1000 → 100,000 ohms, voltage amplif. = 3 fans → 10,000, & R of recording galvan. = 1,000 & 10,000 ohms.

Recom. amplif. usable either 6 or 4 stages accdg amplif. desired.

1st 5 stages employ 239-A tubes, & final 6th stage 205-D tube

Amp. assembled & mounted by Mr. Rand. Martin

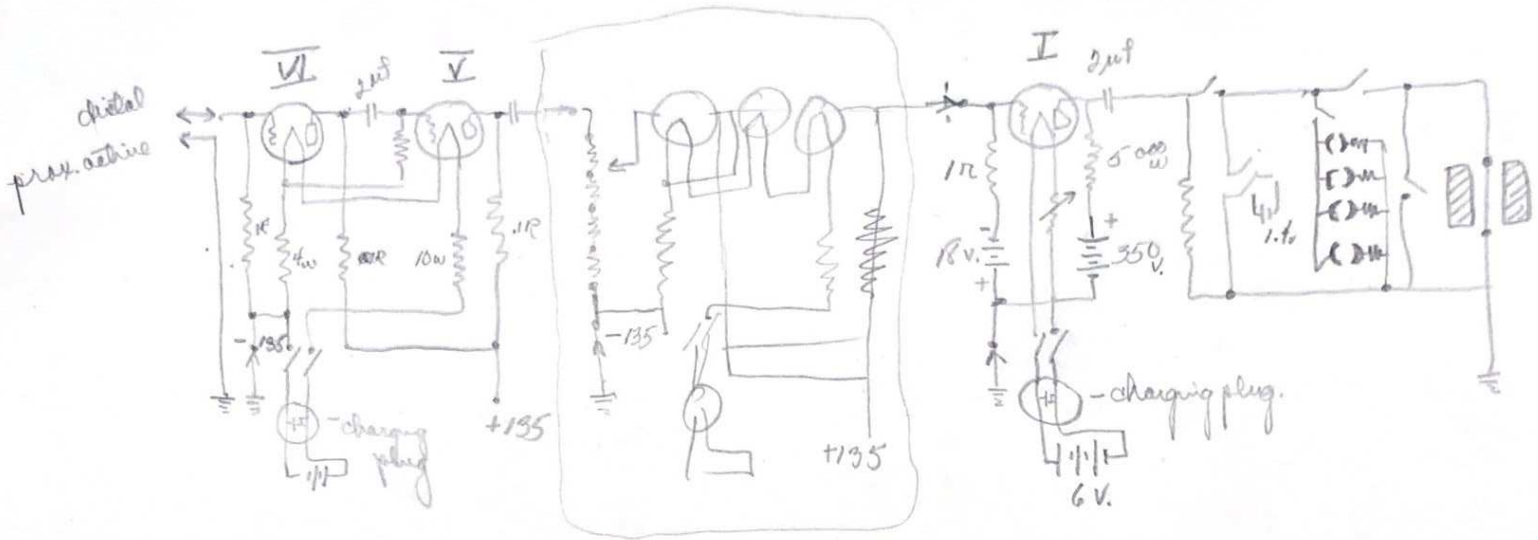
Built in 3 units 1st 2 stg, 2nd 3 stg, 3rd, power stage.

Each unit in independent box w. indep. groundg & batteries.

Tubes mounted on pieces of lead 5 mm. thick, set on pads of sponge rubber. Tubes steadied by rubber bands passing to vertical supporting parts

Wooden boxes containing the amplif. units, stand on a thick piece of felt in a cabinet in the galvan. pillar. Latter built from its foundation indpendent of the building. Inside of cabinet is lined w. laminated sheet iron & shield against elect & mag. & doors have celotex layer in addition to guard vs. sound wave dist.

Ampl. Davis – for short high tension string galvanom.



Qu'est-ce que c'est un gene?

Maybe a gene is a small glob of a particular chemical in a cell which in a certain chemical matrix will react & alter the shape of the cytoplasm.

Cytoplasm & nucleus in chem. balance. When gene gets out on tip of a branch or a finger, maybe the chemical environment is such as to cause reaction of the gene chemical so that it alters character of cell into flower cells or finger-nail cells.

★ Test by growing cells in tissue cultures. Alter the chemical makeup of the tissue culture by extracts of different parts of the organism and thus see if can produce diff't types of cells.

When lumbo sacral region of cord in pups is entirely cut off from afferent impulses by double transection and dorsal root transection, Sr. contin can be elicited by mechanical pressure, jarring, etc of that part of the cord wh. is unprotected by bone as in normal.

Then, there is an organization in the R's. The antagonists don't pull against each other & the distal portions of limb has lower threshold as is the case for spinal reflex. But cord is not autochthonous

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Nov. 18

Effects of nerves on development, maintenance, regeneration of muscles & sense organs.

(Trophic influences)

atrophy vs. degenerat. Power, Rhusted, Parker, Stone

Exp't'l Embryology of the Nervous System

Seminar, Weiss, 1938

The central n. syst. is sheltered under bone, is perfectly static. It innervates the m.s. These have to move just right at the right time. When you say "just right" it means with respect to other parts of the moving periphery – not the central syst.

So in order that the motor organs may be adjusted with respect to the dynamic periphery and environment, then there must be a relation between the periphery & environment and the muscles. i.e. thru afferent n.s – the static system could be infl. no other way.

In other words there must always be an influence on the centers from the sense organs – else the ~~sense org.~~ centers would have no means of adjusting the motor impulses to the periphery & environment.

This is prob. true of human organism – but possibly there are more autonomous mechanisms in the lower vertebrates. Perhaps a central process may be started from afferent impulses and then work itself out, discharging into the periphery meanwhile and unaffected by periphery. Simple locomotion may go off that manner.

Should be able to prove that by getting mechanism going where it wouldn't accomplish results, but would have to be sure that no afferent impulses came in to stop.

If limbs are deafferented? What can the animal do? If he can walk, swim, etc. then there must be some cues coming in to start it off

It's at the start that you could tell whether peripheral factors are influencing or whether it gets going from visual or other cues.

If the process is central, then there must be a central mechanism that mirrors peripheral conditions.

If peripheral condit.s count, they must be inherent affairs 'cause limbs go off w' ~~[illegible]~~ wrong transplanted axes.

Embry. + Expt'l. omit, get neurology. when name work.

Diffic in anatomical + physiol. pt. of view.

Keff figures embryology is going to tell how n. sys. got that way.

He is going to find out how n. syst. works, and is going to shatter many conceptions now current.

Neurobiotaxis is out.

Few engaged in neuroembryology.

Detailed Neuroembryology for text.

Mammals or amphibia:

higher centers, cut off as go down. Caretaker of rats, train 'em.

Where does action-current come in?

He'd train 'em [redacted] and then cut off layers + find out where primitive appears.

Proof of the central pattern, central discharge.

A linkage of molecules that react and are modified.

Note: the impulse travels only over the specific molecules.

The splitting of axones shows that it can't be a matter of connections.

Then show where association has occurred. A matter of operating on rats. Shifting their muscles by the tendons. Then retraining them to use the shifted muscles – after which you cut out the forebrain and on down and see how far have to go to bring out the old associations.

Or graft frog legs to back where they'd do no good + see if they still coördinate.

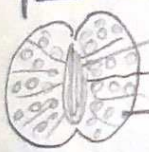
Want something that can work at steadily, put in extra time etc.

Keet.

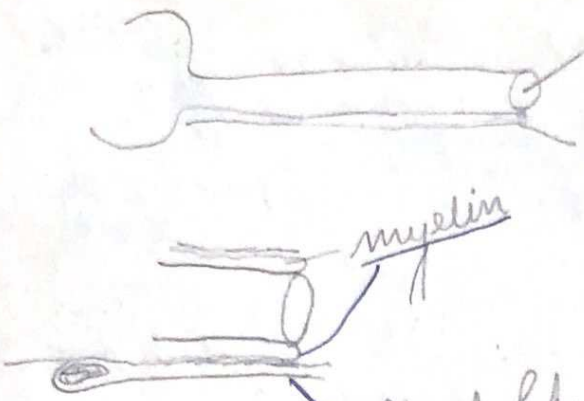
Any part of ectoderm can form nervous system.
Rathke's pouch around hypophysis.
Neural crests migrate out → ganglionic crest.
presumptive cells " .

Proliferation of cells occurs on most ectodermal of surface of neural tube lining of neural tube, brain, etc that proliferation begins after growth starts

Inner and outer limiting membranes holding neural tube plate. Cells of medullary neural plate secrete the supporting membranes.
On proliferation, the tube becomes several layers thick, cells migrate radially rather than longitudinally - don't know why.
ner. syst. is pulled out this way probably passively to great extent.



proliferating layer, later called ependyma.
Some of original lining cells stretch greatly and reach to outer layer serving as support & equal 1st traces of glia.
Spongioblasts later turn into glia - look like regular neuroblasts at 1st.
Astrocytes = partly support, partly nutrition
Nerve fibers begin to develop!



late evidence that all n. cells have a myelin-like coat.

cells of Schwann slide around n. amoeba-like and spread out over it

"sheath cells" surround cell completely.
on all cells.

Myelinated fibers show extent of sheath cells, because a break in myelin under each cell at ends.

Ns sheath cells in centers its place taken by the glia. Schwann cells called peripheral glia.
But there's myelin so myelin from axone itself.

Cells do not contain irrevocable constituents at begining. Parts can be interchanged. muscle + skin interchange. Indeterminacy of cells. Surroundings make tissue what it'll be

Practically any cell early, can form n. syst. Likewise N. cells form any other tissue early enough.

Mesoderm beneath med. plate does something to make med. plate → nerve cord. Has to be in contact.

(Ner. syst. acts now to make ectoderm produce eye, ear, nose etc. = organizers.)

Injure mesoderm on one side and it makes the med. plate develop asymmetrically. Ectoderm plays important part in shaping the n. tube.

Later, however, a certain limit of repair of shape. Morphology of plate. Plate isolated & rolled up like cell. Take in sand. One surface has to contract, the other to expand. Has plastic plate of diff. swelling capacity. Like agar.

Glaser 1912. H_2O content much higher than rest of embryo cells. Before gastrulation they don't take up water. Water taken in — that's why neural ectoderm swells. Colloids swell for many reasons — salts, enzymes, etc. Large conditions there probably that cause differential swelling.

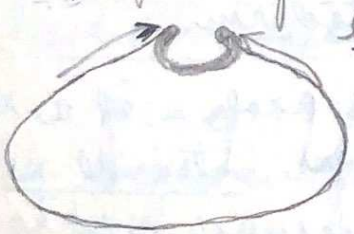
— found that nuclei crowd to bottom of plate — so perhaps greater H_2O content in upper pole of cell.

If grow bent plate in tissue culture, the nuclei crowd to outside.

Bending of plate is autonomous, by itself.

Any how bending of plate may be caused by Greiberg — ectoderm partly. plate will fold if placed in sugar solution? hypertonic condition dehydrates

ectoderm pushes slightly.



Symposium

Devel. of Behavior w. neural correlates.

1) Nature vs. Required
2) Neural correlates of embryonic bhr
→ 3) Effects of n. syst. on development, regeneration

Dependence of n. syst. on milieu – not autonomous substrat of mesod.

Lehmann – indicates lateral aspects of n. syst. correlated w. mesod.

Adelmann – 2 eyes fuse, etc. depend on mesoderm.

[We don't know what sort of an effect the mesod has.

Hypertonic sugar & NaCl solution causes n. plate to stiffen and doesn't close = spina bifida occasional human birth, sometimes animal lives quite a while.

Surprisingly little disturbance of behavior pattern

How much morphology of n. syst. characterizes behavior

1) Defects in surrounding mesod.
2) " " closure of tube.

2 synergic factors operate

a. Autogenous rolling ? don't know why
b. Pressure of lateral ectoderm.

[After rolling n. syst. assumes shape of a retort would collapse if it were not for internal pressure.

Hypertonic fluid inside = pressure of cerebro-spinal fluid.

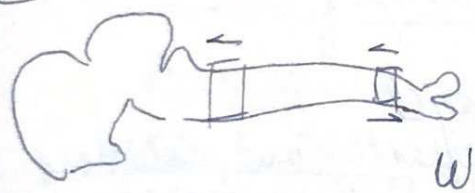
In remaining, outline W.'s courses.

Studnicka - Cells lining the canal show secretory activity wh. later is restricted to choroid plexus. = membrane reach into ventricles, like sac for chem. dialysis. Some sort of filtration goes on - "haemato-encephalitic barrier" true secretion also going on.

General char. of embryology · gen-spec. areas per tissue

Expt. on chick meninges

cut out a fragment of n. cord and cut into 2 halves of inner & outer. & transplant into blood plasma. The inner mass will soon be surrounded by aura of exudation. Outside piece just sticks in coagulum.



Liquid is propelled anteriorly by cilia.

When a portion of cord transplanted from anterior to posterior — orientation normal, switched there was a collection of liquid at back end. Liquid pressure actually caused it to push out.

If liquid prop. forward it helps to extend the brain ventricles.

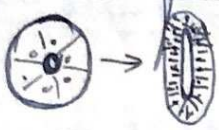
3rd factor in development of tube

You can hardly keep a mass of transplanted n. tissue from developing canals in it — due to cells lining that secrete - cyclostomes + fishes develop from a solid n. syst.

Recesses = folds in walls,
Differences in thickness of walls.
Growth pattern of n. syst.

(We know not why certain parts of organism grow at more rapid pace than other.)

Growth of neural tube:



possible there's a syncytium in the nerve cord.
only cells close to lumen show mitotic figures.

Growth factors rate & direction

fewer cells could mitote if lumen were round, slit gives more surface.

cells that migrate to outside don't divide any more.

(cells add to thickness, not length of tube)

No central control among these factors

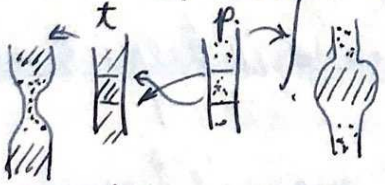
1. Shape of canal

Rel. to notoch. under N. syst.

neural tuel lies directly on notochord.

muscle repels lumen

A. p. & A. t. exchange pieces of sp. cd. at stage when they're alike



holds for early stages – later they even up to correct proportion

so, intensity of mitosis is an inherent factor of tissue

There is a mitotic pattern – close to canal.

same factor in liquid probably S's cells lining it to divide.

There are distinct foci of mitotic activity along the cord.
(Coghill) has done considerable work on this subject.
At 1st uniform, then brain comes in w. tremendous peaks at points. At pt.s there is shrinkage which indicates migration of cells & shows that shape of n. syst is not due entirely to rate of growth.

(Burr) has studied mitotic patterns also. Get evanescent foci of growth.

① Rate of growth, ② Migration effect mass of cells at any point.

In brain:

(Frank) In bulges, there's rapid mitosis wh. causes surface expansion, cause don't migrate.

Cells lured away from canal to outer portions of tube causes thickness of tube.

ependyma cells that form lines along wh. other neuroblasts slide out.

(Zacharias) cf'd dev. by cutting out segments & transplg them elsewhere in body, but don't connect.s to tube.

N. syst. has no tendency to grow in length, lags behind body-growth = passively-lengthened. Transplant beside cord is much thicker than normal in the cord & cell count is the same, but that in the tube is passively stretched.

How does stretching occur?

Tube is motile, doesn't stick to anything

But is firmly imbedded in mesenchyme & tail bud and anchored near ant. end of notochord by cervical flexure.

We know little of longit. shortening in ms. cyst

What makes cell migrate toward periphery?

Electrical factors suggested

Verworn has shown protozoa orient & move toward electrode in ms current.

galvanotaxis.

Probably a diff in potent. between outside of tube & inside

Ariens Kappers suggested cells move out in the field of electrical radiance

neuroblasts in tissue culture were disappointing.

Peterfi & Kapel & Williams usually elect. current were lethal. in sub-lethal doses cells appeared to orient a bit. Neuroblasts in elect. field may possibly move in an electrical field. (Fe blasts, not fibers)

2nd sugg. Weiss favors + ependymal fibers form a mechanical structure over which cells glide out.

Assignments Nov. 18th or 22nd Effect of nerves on other tissue

Point that we go after stuff ourselves. Come in and ask him questions.

(Neurohumors - no.'s that can grow in - etc. all only in so far as it effects behavior.

How do these mitotic foci arise? - cause? a general problem of development.

Growth pattern intrinsic to certain extent, but nerves only as base-line on wh. other factors are imposed.

2ndary factors, partly peripheral & partly intracentral.

Length - passive, width - active.

Folding centers & Rind link centers appear before growth of buds appears.

? (

Neural crest split into 2 lateral crests down beside cord. looks as tho it were pared down and dripping around cord - just columns whose segmentation will come later. They form dorsal ganglia & sympathetic (partly) and contribute frame to sheath cells around cord.

Segmt'n of ganglia:

1. Depends on segmt'n of myotomes. Neural crest wedged in between myotomes and neural cord also begins to show segmentation. The crest column breaks up more or less irregularly, but one to each myotome.

Lehmann was 1st to study relation, when myotomes are removed, the ganglia don't segment, nor do neural arches.

Detwiler 1937. As dripping down occurs, the neural arches step it in places so between-drips = ganglia tendency to break up into clusters w'out myotome, myotomes merely arrange it in regular manner.

segmt.s ob'tomes in place of 3 causes # neural crests. But W. thinks can go further and say it's the neural arches which crowd out the neural crest in segmt.s. N. arches deranged as much as ganglia by derangement of myotomes.

1. N. syst. develops 1st in center w/out connection periphery.
2. Then suddenly mechanism of connection up w. the periphery begins. i.e. nerve fibers begin to develop.

The dev. of n. fiber acquired much attention & ne. syst. is organizer par excellence of organism.

Survey of history of debates concerning.

1. Organism controlled by organism – no primary control in n. syst. Said n. fibers develop. along pre-invisible tracts.

2. Secondary origin:

a) One school – cell chain theory Lehmann 1839
Balfour, Dohrn, Kupffer.
Thought n. fiber = chain of cells, not one cell, but a pipe-line of cells. How built? what pipes
① Myelinated fiber show segments. figured that each cell developed in place from peripheral & central neuroblasts
① of central origin
② neuroblasts of periph. "

b) Outgrowth theory + Schleider, 1857 His 1886-90
fiber grows out from central cells.
① His grows from single source
② Impulse travels out that transforms material in its path into neural cells
Held assumed plasmodesms = plasm connections between all cells – so influence spread out from the centers.
Held suggested some fibril grows out, but that it follows plasmodesms

So got down to having origin in centers, sometimes had to emanate from centers.

I

novelties
↓
Ramón y Cajal
Kölliker

~~Bonnen~~ Could it decide this question by histological technique
Braus & Harrison both in Germany ?

Harrison for Hist & Braus for peripheral

Do nerves w/in limb arise if limb or in centers?
pattern of " " " " " " "

When transplanted to foreign part. as eye, etc. the limb got typical limb pattern. / so.

① Braus said nerves must arise in limb.

② Harrison, doing same, concluded they grew out, but followed factors in limb that guided 'em into their patterns

Harrison went on cut out part of spinal cord & filled it w. ~~blood~~ coagulated blood. Found it pervaded w. N. fibers that had root in nearby cord.
Grew nerves in vitro. Created the method of tissue culture (Weiss just appos. to Harrison in question of technique.)
Clot of blood on slide w. neuroblasts - few cell sprouts came out & w/in a day or so grew out.

Aug 1935 Proc. Roy. Soc. of London Ser. B no. 808 v 118 p 155-196

Where nerve fibers were naked, however, as have a diff't source for sheath cells, viz. come from neural crest in early stages. (Here misled early advocates of chain theory.)

Harrison showed this by removing crests & dorsal neural tube & got bare fibers out into muscle.

Harrison 1908 1st observed N. fibers growing out in tadpole tail.
Williams stained fibers and showed 'em up better.
Speidel watched N. f.. in tadpole.
(J. Exp Zool v 57 1930 Williams not too good)

Amoeboid growth at tip of N. fiber. Perhaps material is synthesized in cell body, perhaps in axone we don't know how much of each - both occur.

Tip is active rest of cell is passive. Sheath cells then put on and if to be myelinated, later. * * came in quite irregularly & keep dividing in periphery after leaving crests.

Whether myelin to be formed or not depends on character of nerve fiber. Of course needs presence of sheath cells. Probably myelin formed from the nerve fiber itself. Speidel had some lymph cells between myelin and sheath cells.

When does fiber remain single and when does it branch?  Pseudopodia feel their way forward as in amoeba. After one established, flow accepts into it & is withdrawn from others.

(cf. water on table - drawn out one long branch & other dries up)  dams up in front of obstacle for time, then pseudo go around and maybe both currents persist and maybe one drains all.

High ramification of dendrites & axons from obstacle?

— Sometimes get an offshoot of an older nerve = collaterals produced by irritation or injury.

Speidel J. C. Neur. v. 61. no1. 1935 & refs.
" Am. J. Anat. v 52 1933

Nerve fiber can be spun out - elasticity of a nerve cell is enormous (?)

Something transmitted from cell body & periphery. We know that certain nerves & glands taking each

be carried out along nerve - don't mean carried along nerve axons - interstices & lymphatic spaces between nerves fibers that may be the place of transportation.

Parker has insisted on transport of substances inside of axon. Question open. We don't know. (influence of central cells.)

Report of facts - discussion of facts.

Roger's stuff - work that is homelow. I have the start.

degen & atrophy degeneration vs. no degeneration.

Cajal nerves grows out in regeneration ½ - ¼ mm/day in the year mammals. Harrison tissue culture ⅓ /day, Weiss 1/mm./day

Regeneration in human beings - # mm/day. dependent on temp.

Morrison has measured accurately

C 26°	2.5 mm/hr. (?)
39°	33. .. ..
41°	21.
43°	29
46°	8.7

Few figures for growth in embryo

2½ = in the cords

4.1 mm./day = in vivo

1,5 - 6 mm./day in cords

Summary of nerve regeneration

1st outgrowth of neuroblast = axone cause or effect.

except where have bipolar in spinal ganglion cell.

W. doesn't like to consider the spin. gang. as ~~axons~~ dendritic

traditional story of the growth of spinal gang.

W. says no function in neck of Y.

axon — axon.

Declares there are antidromic impulses that go efferently over sensory processes to blood vessels.

Sheath cells around axons and myelin or no myelin - In centers may have myelin or no myelin.

Nerve pattern of adult organism. — bundles of periph. ns are of 2ndary origin. primary = axons.

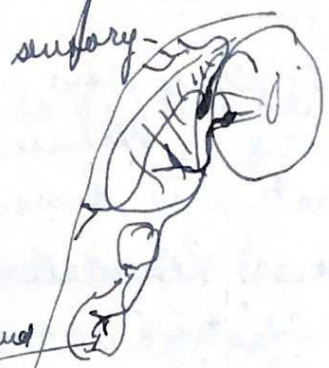
Plexus formation, fusion etc. = 2ndary.

Distances from center to periph. = very short in embryo.

Neuroblasts get thru membrane of nerve cord (same how)

The muscle myotome is right there and at that early period a single neurone innervates each the myotome & then the myotome can twitch

Lateral plate thickens to limb bud & is innervated the mostly cartilage



Motor side develops 1st long before there's any sensory impulses — so W. says its autochthonous. no reflex.

(In lateral plate the neural connections made before m. cells actually differentiated. m. masses probably

When thus get anchored, pulled out at each end. passively

M.s of body wall from myotomes.

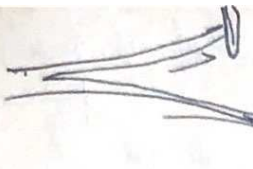
Further course of nerves = passive distortion. Thread left behind to track migration of the m. grps.

Fins of fishes that migrate anteriorly carry nerves from way behind.

M. of diaphragm show migr.

Nerves are taken in tow by the m.s

Limb buds form from mesenchyme. Nerve pattern in limb retraces migrat.n of limb muscles.



Get branching so. Connective tissue comes and wraps around the bundles of axones.

So a 2ndary process.

1st fibers that innervate a structure = path finders or pioneering fibers. Further innervation and these late-comers follow the old paths. The nerves may stop or go on to new structures.

Shifting of central cells, migration, that distorts the primary fibers.

Growth into periphery of large animals. not single-handed - needs help of sheath cells.

When an axone interrupted, operation

1 local irritation traumatic shock
2 degeneration - effects periph. & central stump differently.
3 regeneration

"central stump" = nearest cell body.

peripheral degenerates & central remains.

Degeneration is queer in nerve = vital phenomena w. production of new substances

peripheral end apparat. first undergoes degeneration. due to lack of impulses in motor wh. about sensory?

Myelin sheath breaks down & lymphocytes digest it. Axis cylinder breaks down. Whole area fills w. vacuoles & tissue débris.

Progressive changes occur in the Schwann cells - nuclei divide, protoplasm contracts back around nucleus + synthesis of Schwann cytoplasm.

Get a tube of vacuolated mass w. the nuclei of the schwann cells in it.

The central part of n. fiber no longer functions

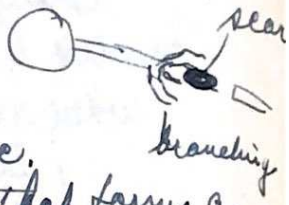
Protoplasmic syncytial band left in old n. path called Buengner.

Proximal part = O.K. traumatic shock usually does not go more than sheath cell or two no changes in cell body also nerve fibers break down
Wallerian degeneration. (?)

The cell body itself is affected, nissl bodies, chromatin, very gradually degenerate

Ascending degeneration = Gudden's degen. used in tracing central pathways.

A new outgrowth begins at cut end.



Nerves w. connective tissue are elastic.

A scar is left in gap where old cell was that forms a link between prox. & periph. parts of axones.

Get a "growth cone" of branchings about the scar.

do single axons branch? or is it the nerve trunk?

Clubs formed at ends of regenerating branches in scar

Growth cones sheaf out & traverse scar in all directions

Neuroma of strayed fibers that get lost in scar tissue & develop sensory endings - pain after n. operations.

Those that find old degenerated path sheaf ahead rapidly. form healthy nerves, others = freaks.

In absence of old degenerated paths, nerves may grow, but very slowly

Growth varies in type of nerve

radial	4-5 mm	/ day
ulnar	1.5-2	"
median	2-4.5	"

Seems to correlate w. certain functional values. excitability

same trace of old quant. diff. left in the sheath paths, he says, but. — of later

Mech. & chem & freezing etc. causes same type of degen. & regenerat. Dietary degeneration in beri-beri causes degenerat. of periph. N.S — regeneration occurs more smoothly.

Handbuch der Neurologie - 1935 J. Boeke
Nervenregeneration

Thinner fibers degenerate faster than thicker

Speed of degeneration varies in the animals.

Summer frog 30-40 days degenerat
Winter " 120+ " " (60 days better)

Birds - 2 days
Mammal 4-5 days depending on age of animal.

Most authors studied physiologically. S. & watch m. but end-plate breaks down very soon. Act. pot. Titrea has got A.C. & studied the decrease after the operation

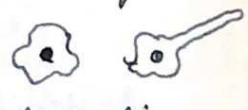
Two weeks after the transection still got A.C. in the peripheral portion 3 weeks still get some a.c. but 5
1 " to cut.

Protoplasm of N. fibers thru intern. protopl. bands of Buengner. Individualization occurs later out of the common protoplasmic mass. Then have pulled over starting from the periphery. So the N.S may modify the nerves peripherally so that can't say peripheral outgrowth is random.

Anastamoses are very frequent. Work this into seminar paper. No " are of the individual axones.

Do the nerve organs regenerate? apparently they do in adult, such not in embryo.

Prob. of orientation of path of nerve fiber growing out.
"Electrical, chemical factors" = evasive statements of literature.
Nerve pattern qu'est-ce que c'est? Sensory fiber pathways growing in, are not pulled out passively as to muscles.
The nerve trunks seemed to be "normed" in no. & size
Lead poisoning causes "radial" nerves to drop. Inf. paralysis goes to motor cells, tabes affects dorsal tracts.
Adrenalin affects sympathetic nerves, acetylcholine affects parasympathetic.
So there are chemical differentials in the nervous syst.

Orientation of n. fiber as it grows out:
Electric effect on polar axis of nerve fiber? 
Something may irritate cell to set out a pseudopodium.
Cells do it in tissue culture so maybe not external forces.
Something causes weak place in cell wall. Possibly an electrical factor, change of surface potential at one point.
Axone always grows out at the far end of the cell.
(What about intermuscial cells?)
Why does neuroblast move?
Ariens Kappers suggests neurobiotaxis, that neuroblast in a certain direction when a S. hits it. Based on phylogenetic morphology & translated into ontogenetic terms. It fits mark so in ontogeny.
Functional S. plays very little part in devel. of the nerv. syst. ?? in man??
S. to nerve growth like S. to ear growth.
Neurobiotaxis means nothing but Kappers has put electricity as the S. = electrobiotaxis.

migration of neuroblast direction of outgrowing pseudopod, direction of the fiber after getting a start ? ? ? ?

Older nerves use the older nerves as a guide to their goal.

1 2 Certain types of fibers connect up with certain type of end organs.?

Nerve fibers grow out w/out any idea as to what end organs they're to connect up with.

Diff't nuclei of the CNS are connected up w. definite other nuclei. The specificity of neural connections.

The direction of outgrowth of the peripheral fibers:

Either orientation from start or a general mess at first out of which the regular trunks last. (Like blood vessels sept. of thick) gradual elaboration. Some evidence that there is a little over production of nerve fiber.

So nerves must grow out w. definite orientation at the beginning.

Orientation of nerve fiber? Is fiber endowed w. guiding factors or is it passively deflected.?

Tissue culture shows N. fiber growing out all any & every way. So it's mechanically or otherwise deflected passively.

In frog, spinal segments of cord are shorter than corresp. segments of the body, thus caudal equina. = expression of lag of growth rate of cord & rest of body. It's otherwise in the Selachia, however.

Arm innervation in 4, 3, 4, 5 segments. Ostwiles using tail-bud stage moved anterior limb 3 seg's back so takes 6, 7, 8 segments. Spinal nerves on other side. Tendency of the brachial nerves to be attracted to the new location. Innervat. = 5, 6, 7 or so. Same thing happened when moved forward so 4321 innervate it.

Not the same brachial plexus but new one. However, a tendency - that said nerves attracted from a distance.

If done in later stage, there's no differentiation.

Like Nasal placode in same region and get a

convergence of a nerve toward the placode, use tail bud + also get convergence toward it till get to the base of the tail bud but they do not penetrate into the tail bud. So primary orienting factors are separate from those that determine final connections w. periph. organs. Converge toward eyes somewhat.

There is some sort of general attraction that works toward any part-growing path. Older ones don't work.

Kuntz worked on olfactory n. wh. grows in from periph placode grafted back. N. fibers grew back toward brain & finally perforate brain. He studied earlier stages. The ingrowing fibers seemed to run along meninges until they came to spot of high mitotic activity & then they moved into the area. This up w. Ariens Kappers's work.

Olf. n. grows in + some organs

One nucleus ties up w. another in the brain, because centers develop at one time tie up w. each other. Sometimes in one direction, sometimes in both. Cajal says this, but he doesn't make clear whether he means mitotic centers, or ~~metabolic ones~~ differentiating fibers.

Ant.-post. gradient in outgrowth of spinal nerves. so the nerves that innervate the limb are those that are growing out when the limb bud is developing.

So nerves attracted. — Ties up w. regeneration of nerves. First they grow in a mass then become more orderly - neurotropism tropism = growth of tip, taxis is OK for moving whole. Cajal - chemotropism

Forman working in reg. of adult amnion.

Degener. paths of old nerves seem to attract the regen. fibers

Interpret the attraction?

His — guided mechanically along w. blood vessels.

Vanlair + ff. path of minor resistance

Pfeffer -

like fern sperm wh. are attracted by malic acid. = chemotropism
Capel interpreted all on same basis = neurotropism = trophism
Same substance diffuses out & nerves R. very delicately to this concentration gradient. diff.'n of Chemotropism.

But a diffusion gradient could guide them only if it is steady during outgrowth. Diff.n in jellies is slow, however. What's more all the tissue are differing so n. fibers must have a specific sense. What's more body fluids are not stagnant & currents might be misleading. Pulse of arteries, flow of lymph, et all produce currents.

Possibility of elect. current. Body potentials maintained only by membranes that keep charges apart. These membranes distort the electrical field that might be set up. Diff't capacities & resistances etc.

Nobody has shown any influence of elect. fields on outgrowth of n. fibers.

Nerves grow in opposs. direct. at same time in brain. Speidel has seen two nerve fiber's tips growing opposite to each other.

2 factors — the growth energy of the nerve & environmental guides

Strasser & Child Rose supported elect. theory.

Nerves are directed — certain factors "attract" 'em.

Nerves directed, attracted toward jellies, agar, etc. soaked in organ extracts — brain substance, best not into spleen extract or liver extract (not good expt, however, a flaw)

The place toward wh. they're attracted is not specific.

Harrison noted mesenchyme cells tend to creep along solid surfaces in tissue cultures — along spider webs = thigmotaxis

No analysis of thigmotaxis yet — to boundaries intersfaces — so possibly surface tension. funct. prop.

H. sugg'd ner fiber might do it, tried it, had no success different tho technique.

Held & others — plasmodesmid & outgrowth theories complete said n.s grew out along between cells already established

fiber net of Sq illy = artifact but there is c colloidal mass around n. cord. Held observed that n. fibers always penetrated along fiber surface. so Harrison's ideas gained wt.

Meantime tissue-culture method perfected. Burrows in vitro's blood fibrin clot. Carrel, fed blood clots. [he did not orig. tiss cult. method] Small amt of embryonic juice that transfers fibrinogen to fibrin.

Harrison, Hanks's cultivated in liquid med. bouillon had to use coverslip as struct. base.

Studied sympathetic fiber as grew out used regeneration ← Levi, Burroughs Ingebritsen.

Levi's art. on tissue culture - good - Erg. Anat. & Entw. Geschichte 1934

N. fibers in vitro - proof of existence of neurofibrils by tissue culture technique.

Been claimed as artifacts of fixation. But in invert.s lobster & crustacea and see objection that due injury.

// rodlets from light. Wang studied sp. gang. cells watched in grow of chick in vitro & see the neurofibrils. Levi & Meyer corroborated so no further doubt there are neurofibrils. Do the diff't fibrils go out separate branches.

At Yale, 1931 Weiss - favored contact relations of Harrison earlier found blood plasma (= phasic colloid) consists of ~~round~~ rod shaped rodlets wh. under stress aggregate to form a spongy fibr mass oriented in one direction. Pull on mesh, cloth. Do that to blood plasma & they'll orient so, and then the cells ff. these rodlet rails

Molecules arrange selves like stake on a fence at the surface -

diff. end of malee. outside than in.

Tensions orient the ultramicrones in slides very obviously - stretch the blood clot culture.

The oriented coagulum polarizes light & orients Oriented substratum. like mesenark drawn out.

The amoeboid tip ff's the lines like mesenchyme ms wh. bodies. Neuroblasts can be thus drawn out by the elastic axone.

Tension is applied early while clot is forming, same while ms is growing on

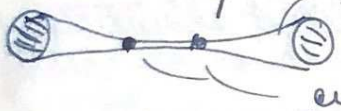
Same thing for mesenchyme cells & sheath cells.

N. tips so oriented in growth. — Orienting agents must then lay down such substratums to guide 'em.

Limb buds, centers in brain, etc. must affect the substrate.

Can duplicate some of this in vitro.

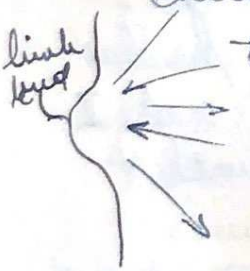
Let growing cells orient the substratum.



cultures to produce both cells & ner. fibers

In proliferating cells dehydrate the surrounding colloids leading to condensation

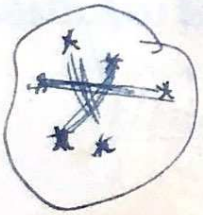
Such a local dehydration in a membrane !!!! causes contraction in that place Two centers of contract in causes tension between 'em.



Limb bud orients the micelli

Kappers & Coghill's law of synchronously oscillating centers of brain are inter connected. down spin cord?

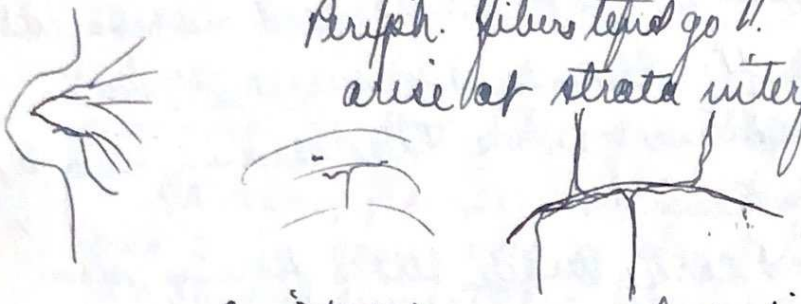
After pioneer threads laid down, you've got a whole system of patterns



Pattern of n.s. like photog. plate exposed several times & shown at once. (Optic chiasma how does it become crossed)

Anastomosing & plexus formation

Brush. fibers tend go ∥. Others converge. Plexuses at interfaces in tissues, retina, etc



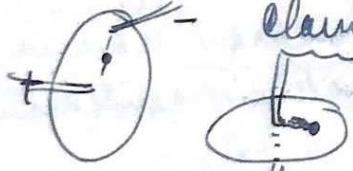
Oriented tension - dehydration
" currents

Principal growing tip of tadpole - conn. tissue ⊥ to surface water changes - oriented currents

Vesicular organs small tension is tangential but there are many canals running radial into vesicle guide n.s

Chem. factors so far no effect. He's tried it in tissue cultures unless the chem. action affected structure of medium.

Electric effects. none so far in vitro Ingvar in Harrison's lab in 1920. Medical neurologist claims growth in lines of current.



N. fibers grow toward conductor & there is no physical force this way.

He tries for two years to make I affect growth & no go. Gray, Speidel & others have found no effect.

Wick electrodes used by Ingvar - sucks liquid, get dehydration tension.

Much negative evidence for electrical effect.

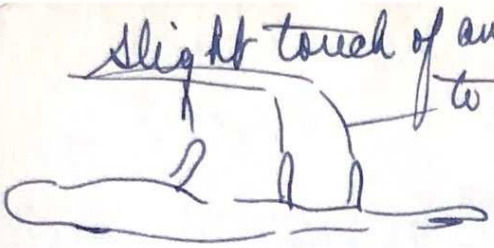
attg a nerve

2) Possibly via sensory nerves.

Remove sensory central spinal ganglia
Obtain same phenomena by grafting a T on
a deafferented plexus.

Coördinations of periph. actions = central affair.
Old ideas based on connections, but this not necessary so long as a m. attached to a nerve that goes into those centers.
M's respond according to their name + always.
C.n.s. has specific type of discharge for each muscle what about smooth mi. Cardiac, sm.'s etc.? Dif. modalities in the c.n.s.
Since there are thousands of neurones, it's an economical means of dealing w. coördinations.
As span as m. is visibly functioning it contracts homologously.
Mo pit.s of no use to the animal itself.
Transplantation of supernumerary m.s into the back of toad

Transplanted from same animals, from other leg.
M. placed so it can't move the skeleton it must be stretched cause can't contract
Use the 8th n. or n. from tibial so know it has no gastroc. fiber
M. twitches on accession in place — then prepared physiologically.
Got homologues R. — even w. nerves that merit limb nerves.

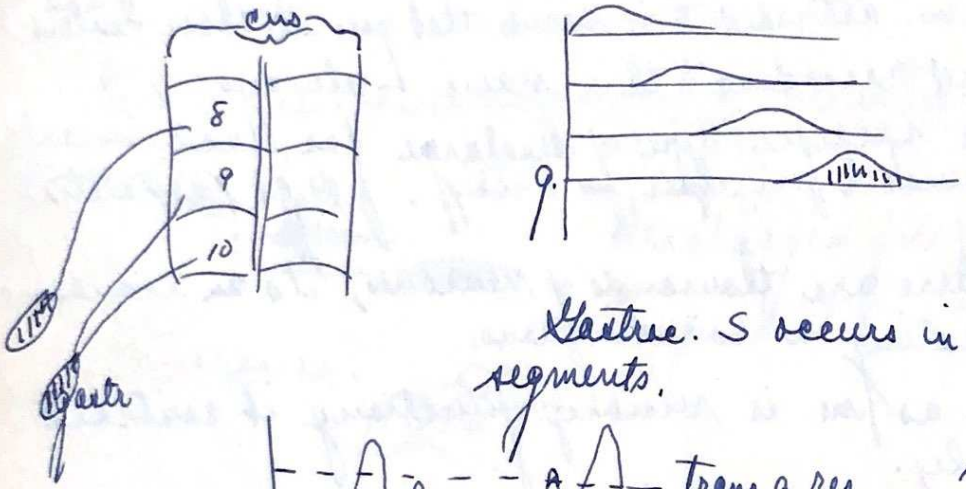


Touch annul & get reflexes

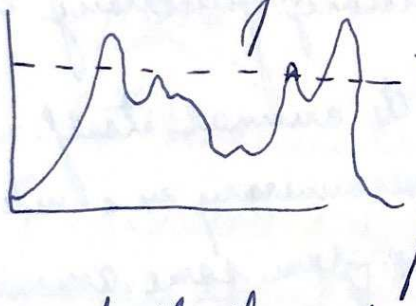
Two m's transplanted to back & 2 diff t. m's pricked out to innervate the latter.

Intensity as well as temporal coincidence.

S. on one side brings stronger R on that side than on contralateral.



Gastric. S occurs in both 8th + 9th - 10th segments.



so a pattern discharged in c.n.s. & more or less of m. fibers are recruited under its influence.

The cns bathes the centers w. these different specific exciting agents & they R. according to receptivity.

Where the selectivity takes place: in the centers.

At 1st the m's contain merely unspecific fibers that contract to any c n s excit - gradually the R. becomes more specific - w. fewer of these unruly fibers.

1. S spread out area motor n's to m's.
selective reception may occur in periphery.
Resonance of m. to the excitation
physical or chemical differentials
enzymes built so they'll work on only one
type of chemical ~~part~~ material.

a) If so, there's no reason why there should be any inespecific R's.

b) Test with afferent-currents.

Wiersma in Adrian's lab. in England tried it out at Weiss's direction. suggestion- but found that motor n.s generally go off when their m's go off.
That is, the apportionment has occurred in the motor nerve already.

So muscle modulates the motor nerve.

A nerve can be varied several times to diff m's in amphibia & each time get homologous R.

Course the specification takes.

Possibly the modulation goes farther than the motor cell. The motor fibers must have access to tangled neuropile of grey matter

Requires only few days to modulate a nerve in the Axolotl, but requires some time in an adult toad 9 mo.s or more sometimes - mere commissure contractions - not learned

Normal amphibia ns. old toads, young toads will show the specification.

Antibody-antibody reactions. Antibody affects protein so it gets other structure.

Sometimes takes several weeks for the convulsive reactions to gradually fade out if homologous R. come in.

Sensory field:

Do spinalar relat.s hold on the sensory side.

Specific functional relat'n between cerebral R.s & sensory excitation.

Substitute simple R's for observat'n of c.n.s. action

Holds for all the diff't n's in the limb. Get homologous R. of myotatic reflexes in 3-legged natural toad, Rana w. bandaged stump & with cornea reflex.

(The excitation may be of some type or comm.s)

Cornea reflex of Amphibia – S causes lid-closure reflex. — may also turn away etc.

M. behind eye-ball wh. pulls it in & lids close mechanically.

Cyclops. cornea transplanted to ear reg. so innerv. from VII facial rather than trigem.

The reflex appears only after metamorphosis.

The transplanted eye has no M. so it doesn't retract but somehow the S to c.n.s. is specific for eye retractor muscle.

Don't get the Refl. when touch other side in same place – / transp. eye w'out cornea & don't get it.

2 cases where it holds on the sensory side.

Reflex tracts thru the c.n.s. that are qualitatively diff't?

Holds for automatic activities of supernumerary fingers of a girl when blind-folded she got the various fingers mixed to tactile cues – gradually learned to identify

Skin may be a little diff't. space, distance, & position count
Same cake in insects where it holds.

If it's the quality of discharge that counts, then habit formation must be same thing.

Same reflexes hard to get cause they don't all go into same other m. — hard to see the limited.
axone is specified to the branching pt. & commonly on in to cell.
M. has no selectivity functionally
Pain fiber, touch etc. may become what they are because of type of peripheral organ
Holds only for limb muscles & cornea reflex
Mammals have superimposed cortical reflexes.

Inherited vs. Acquired

Ps common to a species
Obs learned in utero — how learn w/out knowledge of results. sucking, maybe general coördinations - don't conflict.
1st moits seem to be spontaneous in C larvae (?), cause they don't RC. to extern. S - only internal, spontaneous.
Began on chick — 1st active moit on 5th day.
then 7th wings, of limbs.
How could even moit coörd.s be learned in the embryo. How know that these moit.s don't just appear when they do?
Guinea pigs (fetus) don't orient in the mother, but do immed by on removal.
Angulo y Gonzalez — studied foetal obs of white rats any chance of operating.

Langworthy on Opossum

Sensory areas become smaller & wh. sucking ℞ occurs — how explain in terms of modulation? How explain in terms of connections.

Chloroform in acetone = chloratone.

Harrison & Carmichael.

Spalding's chick-pecking studies, bound sparrow's wings & found they flew well w. instinct.

Breed & Shepherd

Gesell's twin study supports maturation.

Nicholas reared wild rats side by side w. tame ones in tame mother's uterus & got normal wildness in such wild rats. Conn. & Conn.

Hound dogs reared by shepherd on being taken to field, winced put raced about & acted very houndly.

Cerebral lesions as evidence: (ref's from Miss Bishop)

Stone one dogs, & rat — Carter only in learning?

+ Rogers pigeon — " always " " .

Cats kill rats instinctively? ?

Birds songs are affected by bird society.

Homing instinct of birds & learned

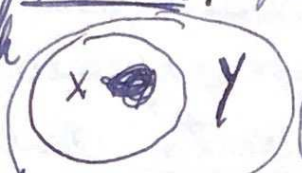
Stone - parabiotic rats & only one wh. had young showed maternal instinct — so not hormonal. Mg-free diet results in lack of " ".

Evidence that learning occurs before birth.

Says isolation is O.K. method. isolate in uterus?

Foolish to ask how much is due to environ. & how much due to innate.

How much of volume of gas is due to temper. & how much due to pressure. The 2 don't interact.

As in growth 

? of whether learning will be possible in utero where no knowledge of results, & no drive or want to learn.

legit.? to ask whether learning can come in.

Can we apply causal syst. to patterns in nature?

Types of order | orbits of order electron

Random — mein das ist es nicht.

Plagge on Coghill. Amblystoma Janet was right.

Behavior problem in Amblystoma — he has no learning of motor coördin.s anyway — so it's merely a problem of how innate stock of reflexes are developed. & of course possibly of how differentiation tracts are laid down wh. may have some functional factors functioning.

Early stages in Ambl. motor n.s innervate muscles in segs. posterior to cell body — goes down cord & out in posterior segments. Unusual — not in higher forms.

Rohon beard cells = same of 'em go into mis name to skin

sensory cells where cell bodies are inside dorsal root of cord rather than in ganglia — don't find 'em in higher vertebrates.

Stages of behavior:

1. Mass-motile
2. Simple flexion
3. Coil
4. S-shape
5. Swimming

No basketball tonite!

S innervation sans motor pattern.
Fish swim OK w/out dorsal roots.
Coghill's reflexes based on idea that m. septds in reflexes from active contraction but there are no cases yet where any active contraction could afferent impulses — only stretch of those m.s.

Have they looked for aff. pulses & failed to get them? — Dempsey Bronk et al / postural reflexes.

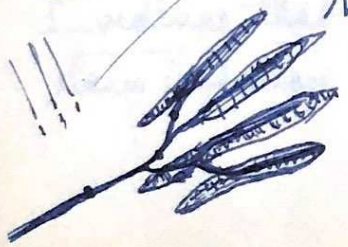
Golgi prep. picks out only a few cells & leaves all others unstained! [The guillotine crack is Bethe]

Coghill's observation support the 4:40
'field theory' of development - nidiv. etc. as much as Hes. denial of learning.

The nidividuation here is merely a matter of nerve tracts being laid down — no peripheral factor.

Rushton has shown that apparent isochronism between n & m. is merely between n. & m. endings in muscle.

Frog's retro-lingual membrane that has m. fibers spread out singly w. m.o



S. a single axone here in diff. region & find that chronaxie varies with the diameter. — so same nerve w. diff. chronaxies values.

Chronaxie is still good measurement of tissue excitability.
Kurick thinks there's too much variation in trying to compare the physiological & anatomical stages (Harrison's) 5:10

grey centers grow in limb regions w. growth of leg
white material increases " motility "

Gal. = a better man. || Coghill vs. Detwiler that incoming fibers cause proliferation.

no correl. between migratory dorsal afferent fibers and grey centers & white substance. on ventral side. 5:16

A. moves his gills about discretely.

Mass ⟶ specific [quality of / minimum mixture]

Could make exact || here of denial of CNS w. denial of the whole embryo.

another point

Child must have been some man to lead so many men so — by.

At 1st impulse spread all over - everywhere there are communications — then how does inhibition of extraneous pathways occur?

Tadpoles' legs are not moved w. trunk muscles even tho they are innervated.

At 1st A. limb mus innervated by collaterals of trunk motor fibers. Later by own motor fibers in limb centers.
Why does limb become dissociated? degenerat.

Angulo - says inhibition maybe - but. Of course Romulogens response answers it. Says collaterals are still there in rat.
Single neurone innervates whole myotome at 1st.

Homologous R. in medusa

Give epithet work & name & organization and will attract attention, workers, criticism.

Embryonic Bhr

Kuo + Windle

Kuo put vaseline on egg membranes wh. makes im transparent Chick

3rd day - head mait.o lifting
↓
6th " - lifting disappeared & get head turning.
↓ twisted trunk
↓ jerking & wriggling mait.
↓ fore limbs w. trunk at 1st.
↓ hind limbs.

Rotation on table increased mait.
Temper. S.

Kuo = psychist at Rochester

Kuo + Coghill at 1st in interpretation.

Ohr (2) Cat.

Found local fore-leg reflex.
Said Coghills' were spontaneous.

Pain reflexes come in all coordinated

Fasciculus = tract
Commissures = always crossing over, ventral there's not much of a dorsal comm. in the cord.

We don't know yet when a nerve cell becomes stainable.

Spontaneous mait.o appear first = integrated.

Can't find any neural correlates.

Windle + Ohr - can't explain spontaneous unilateral Rs — not sure they're neurogenic.

Found motor n.s before sensory.

Muscle is capable of contract in before Rs & neural impulses.

Kuo said inhibited chicks could n't orient as well later on – definitely for learning in egg, not such good evidence.

Amt of adrenalin increases greatly in chick after 5 days.

Metabolic processes mark up to liminal state and then discharges – nerve cells – espec. those of respiration.

myogenic = (skinner) have no latency, (not always maximal) no fatigue period

They don't know whether contr. early are myo- or neuro-

Tracy on toadfish

endogenous - exogenous

Concludes motor - endogenous devel. indep. (of those skates etc. that move about w. in shells)

Spontaneous mov.ts precede S.d. But there is no evidence of neural correlates to explain 'em.

Consider all Coghill's "massive activity" as being myogenic?

Spiedel says embryonic m. does not follow all or none law. and there is no A.C. connected with it.

Then suddenly the whole m. goes off – two mechanisms in a m. (certain strength) the conducting and contracting mechanisms

The action of curare is still not completely understood.

Coghill –

Foetal mov.ts in Mammals

Neural correlates – walking purely spinal in foetal cat – decerebrated. Mov.ts in early foetus = purely spinal.

Langworthy – cats, Angulo rats + showed myelinization doesn't have to precede behavior.

Motor cells before movt.

Progressive segregation of motor cells correlated w. behav. devel.? Limb sp.o show segregation of cells?

Vestibular + other sensory structures present before motor pattern correlated caused this behavior –

Coincidence of devel. of adrenals & movements. Carter.
Recently Yngstrom + acetylcholine esterase appears when motility appears. Possible that adrenalin comes in at time when motility appears. Ca absorbed from chick shell when calcification of frame occurs.

Coghill's opossum work. Observes bkr of somites. + says Rectus abdominis moves ∴ certain neural tracts laid down before at 1st later specific. Move hind legs after being poked 7 days.

Sensory correlates appear w. 1st reflexes.

What about spontaneous movt.s

Offers w in a letter as to onset of motility.

No connection between sensory & motor cells at 1st. When reflexes appear, get connections.

Note that association tracts are laid down last in all cases.

5 mm. Sp. cord reflexes precede massive movt – Windle.
Ipsilateral movt.s precede contralateral.
The simple one-segment reflex pathways are formed 1st.
How get these spontaneous movt.s? if
No spontaneous R's before appearance of reflexes.

Anesthetics

Avery anesthetized + asphyxiated his animals – so –.
Supports Coghillian patterns.
Carmichael + found spontaneous movt.
doesn't support cephalo-caudal appearance of movt.
Intense & fine reflexes, light give massive ???
Angulo 21 days gestation in rats,
Anesthetized 15th day lateral flexion of head on S. = 1st movt.
Get movt.s when umbilical cord cut – nerves or what?
Limb reflexes before trunk movts.

Can get

He's got tables that prove definitely that behavior develops so and so ——.

And "Coghilean" this & that — trying to bring another mis-nomer into the literature.

Windle vs. Coghill & Angulo.

Maybe strong S. will elicit a simple reaction before any light S gives reaction at all.

Human foetal motility — a brain anatomist

Minkowski, Orten, Lapolio Hooker at Univ. of Pittsburgh has moving pictures. Caesarian operations under anesthetics

1st mo. none but heart
2nd " "
3rd w. or m. trunk motility
3rd month — " " + neck rotation
8-10 wks —
end 3rd month — generalized motility
11 wks patellar reflex.

Removal of brain intensifies the reflexes.

5th mo. — grasping reflex strong enough to hold object.
Babkin pupillary reflexes.
Babinski reflex.

5th & 6th mo - S of cortex gives no R.
" " medulla " R of chest, neck, shoulder
so foetus = still spinal.

6th mo. — definite sucking reflex.
— can elicit swallowing

7th mo. — S of cortex no R.
" " medulla R of limb motility

Brain waves start a bit after child is 5-6 mo.s old.

Summary:

Spontaneous activity is never localized - is general.

W. Localized reflexes & spontaneous patterns separate processes

Two distinct processes developing separately - the reflexes & the generalized spontaneous

W. Ask an order in the n. syst. vs. connective system.

V. Habit on running mouse

Vagus to limb — stroke skin — vomiting
few mo.s get relearning. nerve leg → cough

4th type of filter in frog which Rs to dark.

Get a single axon off frog optic nerve & it usually Rs to one wavelength. Hartline.

Spontaneous rhythmic discharges from goldfish respiratory

Compounds get important word in place
Sentence structure.

die die Substanz lösende Flüssigkeit

the liquid wh. dissolves the substance.

die das Leitungsdraht durchströmende Ladung → end = partic

the charge flowing thru the conductor

separable prefixes take lit. meaning

Sci. German

er
blühen to bloom
erblühen to burst into bloom
/ looking back to beginning

ur
uralt very old

aus
denken to think
erdenken to think out
looking to end of action

be (bei, around all sides)
bedenken - to consider
beschneiden cut around. Has intensive or perfective force.
besehen look at carefully.
make an intransitive verb transitive.

ent
over against, in return
entgelten - repay
entblühen - to burst into bloom
inceptive
entschlafen - to fall asleep
separation, removal
enthaupten - behead
entblättern - to deprive of leaves.
entnehmen - to take away
same prefix
emp

fer
prefix forth away
use up in English
fersenden send away
look to beginning or end.
ferblühen fade
ferschwinden to vanish
ferbieten forbid
fergessen forget
ferschlafen oversleep
negation
amiss

zer
asunder, to bits,
zerreisen tear to bits
zerbrechen shatter.

Entfernung = mechanic release
vermisst = miss regret
entfalten = to unfold
berühren = to touch, be contiguous
Kapitel = head, topic, chapter
Behandlung = handling, treatment
weittragender = wide-bearing
Hartnäckigkeit = obstinateness
besonders = peculiar, particular
imstande = able
nachweisen = detect, prove

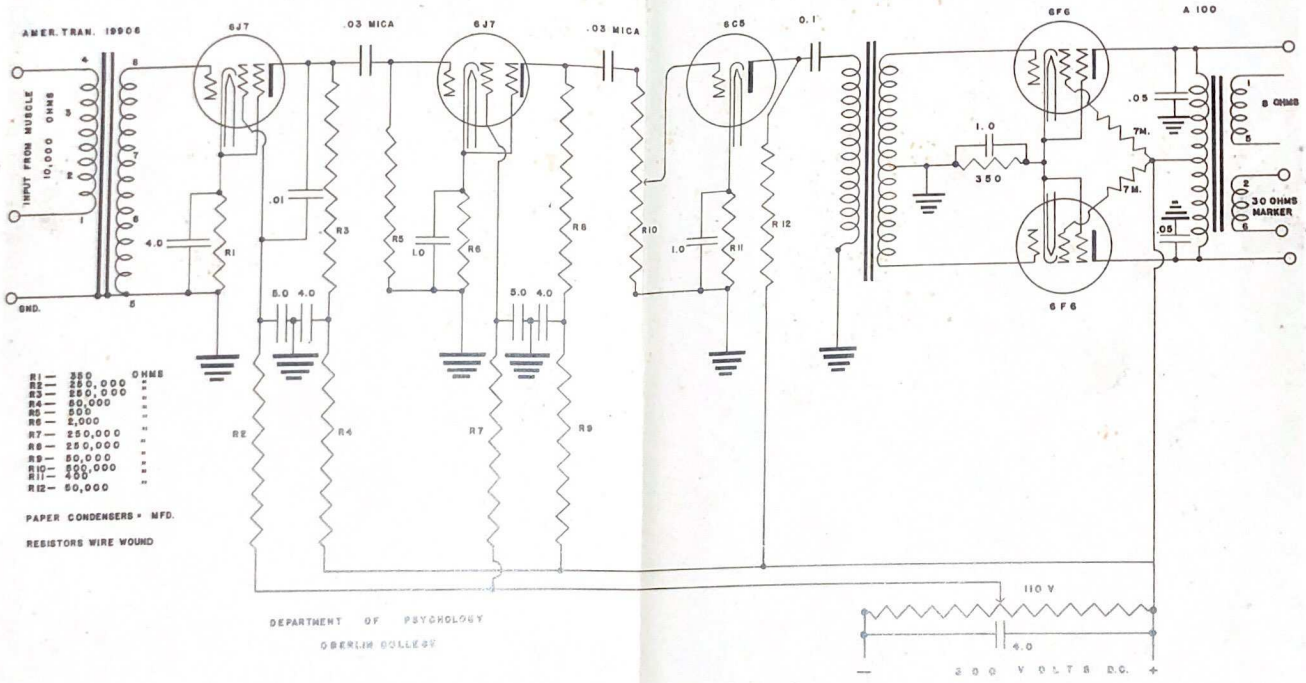
(Zeit. für Orthoped. Chirurgie 1. Bd. Lehrb.)

dauern = to hold out, stand, keep
vollständig = complete, whole, entire
evidente = capable of one explanation
Gegensätzlichkeit = opposition, contrariness
Wortverschiebung = wording - disarrangement
innerhalb = within
darstellen = to present, appear
mannigfaltiger = various, diverse
Einschränkungen = restriction, reservation
Bedingungen = conditioning, stipulating
desto = the, so much
Umständen = conditions, circumstances
sogar = complete
vorschlag = proposal
Verwendung = application
Kraftspendung = skilled-administration
erweise = prove, demonstrate
stillschweigend = still, tacit implying
voraussetzung = supposition
Feststellung = confirmation
bekriegter = defined
Fall = failure
anstrebenden = strive against
Schaffung = conveyance, furnishing, provision
Wettlauf = running race
gipfelte = culminate
Befestigungsart = art of fastening
Hervorkehrung = part appearance shine forth

Hemmung = limit, arrest
Aufstellung = disposition, assertion
Satzes = thesis, proposit
Losbohren = boring attack
zwar = indeed, certainly,
Ursprünglich = source, primitive, original.
verschonen = exempt, excuse, spare
Maß = measure, moderation
Grad = degree
Abstufung = break off, gradations
Befürderung = promote advance
Zeh = toe
Scheide = separation, division
Verschiebung = displacement
erwägen = to weigh, ponder, consider
Erfüllen = accomplish, fill, perform
Aufgabe = problem
Irrtum = error
Ermöglichung = possibility, feasibility
Reparation = repair, mend, heal
Veranlassen = set going, temper, see
antreffen = to light upon
(hin)sichtlich = apparent (toward)
Beweglichkeit = mobility bewegen = to stir
entstehen = to begin, originate
ändern = to ◇
Mitteilungen = communication
aktionsfähiger = action-capable

auffassen - to collect, comprehend
Verfahren - to act, behave, proceed
einheitlich - uniform, unitary.
schaffen - to produce, create
Gesetzmässigkeit - lawfulness
gemeinsame - common, mutual
vikarierenden - to officiate as a prelate's substitute
gebühren = belong, appertain to
zustehen = to unite for a common cause.
gesunden = to recover one's health.
besonders = particular, peculiar, separate.
Abschätzung = estimation
geschädigten = hurt, injured.
u. a. = und anders
erwähnen = to mention, call notice to
weg-fallen = be suppressed, be omitted.
zustehen = unite in common cause.
gedeihen = to increase, prosper, succeed.
begünstigen = to favor, befriend.
hinsichtlich = w. regard to, as to.
Kräfte = force, power
Rückgang = return
zwar = indeed, of course, certainly
ersetzen = repair, compensate
Ersatz = compensation.
bedürfen = be in need of
Eingriff = catching, seizure
Verlust = loss damage
geltend machen = assert,

DIAGRAM OF KYMOGRAPH ACTION CURRENT AMPLIFIER



Neuroembryology U of C 1938
Weiss #5
Notes, refs., comments, German
vocabulary c translation