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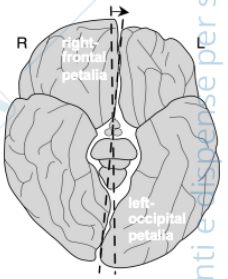
# BRAIN ASYMMETRIES

The brain is characterised by asymmetries: for example, the hemispheres=most macroscopic subdivision in the brain are asymmetric, not equivalent.

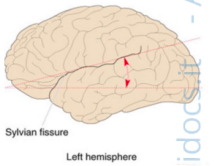
The lateralization index is: (RH-LH)/(RH+LH), where RH=right hemisphere measure.

## Structural asymmetries

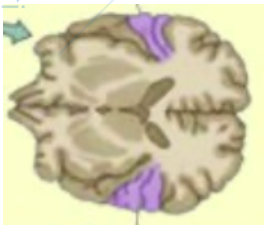
The neuroanatomical/structural asymmetries are:




- Brain/Yakovlevian torque=leftward posterior and rightward anterior rotation, often described as a clockwise rotation
  - in most brain complementary protrusions relative to the other hemisphere -> right frontal and left occipital petalia
    - petalias=protrusions of the surface of one hemisphere, particularly in the right frontal and left occipital lobes
  - microscopically, it's the most evident structural asymmetry observed in the brain→ more pronounced in right handedness




- Sylvian fissure=lateral sulcus that separates the frontal and parietal lobes from the temporal lobe→ longer, less curvilinear and running at a shallower angle in the left hemisphere
  - probably derived from the torque
  - maybe linked to the left dominance for language
- Planum temporale=triangular shaped cortex behind Heschl's gyrus (A1)→ bigger in the left hemisphere (65% of people, vs 10-11% on the right, the rest has it isovolumetric)
  - in some, 5x larger on the left→ most asymmetrical structure
  - linked to language dominance, hosts most of Wernicke's area
    - left lateralization of language (Wada test) → correlation of planum asymmetry and language lateralization
    - dichotic listening: right ear advantage=better reporting on the stimulus if it's held in the right ear, as it projects more to the LH
      - LH language dominance for spoken language and syllable decoding
      - but: not always a correlation between lateralization of language (advantage for contralateral ear) and asymmetry of the planum temporale. Attentional effects?



- White matter asymmetries=some structures are lateralized, probably because of a specific link with function
    - arcuate fasciculus: not strongly left-lateralized as a whole, but its fronto-temporal segment is extremely left-lateralized in both volume and calibre of the fibres
        - the right long segment's volume predicts speech recovery from post-stroke aphasia, or resilience for neurodegeneration
    - cortico-spinal tract and superior cerebellar peduncle: lateralization not linked to lateralized hand preference and manual specialisation
        - not strongly lateralized in the general population
    - fronto-parietal tract: asymmetry in the volume predicts hand preference, in particular the first (dorsal) segment=motor planning and visuospatial/visuomotor integration
        - preference for the contralateral hand to the more developed tract
        - dorsal branch of the superior longitudinal fasciculus (3 branches) typically important for visuospatial integration and motor planning
            - negative laterality index=larger tract volume in left H vs right H
    - → we're different in terms of structural brain connectivity and asymmetry, because can have an impact on the individual trajectory of recovery
- left right asymmetry: could be better predicted by the projection tract and corticospinal tract and/or the superior cerebellar

The anatomical asymmetries may explain the lateralization of specific functions: functional asymmetries are more linked with microstructural features which developed to sustain a specific kind of activity.

We compare the dendritic length and proportion of the dendritic ensemble composed of lower order (first, second, and third) and higher order (fourth, fifth, and sixth) dendritic segments in left and right temporal areas for hearing→ its difference might indicate a difference developed to sustain language comprehension and production. In fact, they're denser in language areas (LH). We can operationalise the complexity of dendritic arborization by counting the branching

Prosody and emotional content are right lateralized

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## Functional asymmetries

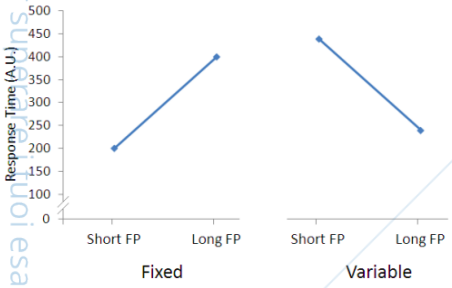
Functional asymmetries/hemispheric dominance/preference/lateralization=tendency for one brain hemisphere to prevail over the other in carrying out a specific brain function, which relies mostly or rarely exclusively on said hemisphere.

Examples of behaviour due to functional brain asymmetry in animals? Footedness in parrots, tail-wagging in dogs, visual perceptual skills in dolphins, schooling in the same direction for fishes (survival)

- Left lateralization
    - language (Broca, Wernicke, Liepmann)
        - apraxia is caused by lesions on the left side, as the left hand-motor area is disconnected from posterior brain regions (Liepmann)
        - apraxia=inability to perform purposeful actions while the overall cognitive profile is intact, more common with left hemispheric lesions
    - handedness:
        - right-hand handedness is given by LH control→ the LH is dominant over RH, which is subaltern in absolute terms (major vs minor)
- Right lateralization→ evidence from split-brain patients+functional neuroimaging
    - processing of non-verbal stimuli (faces, music, abstract form, mental rotation) and paraverbal features (prosody, affective tone recognition)
        - activation of both hemispheres for content-related stimuli, just RH for prosody vs control
            - neuroimaging causation, not correlation: cause-effect relationships are inferred through TMS, split brain patients, focal lesions (quasi-experiments=you don't manipulate the independent variables)
                - demographic features and lesions cannot be manipulated and some external elements can intervene
    - spatial attention:
        - right ventral fronto-parietal network
        - neglect=incapacity to orient the attention towards the left
            - can be dissociated from any other syndrome
            - linked to damage in right posterior parietal cortex or subcortical areas in the fronto-parietal ventral network (even small lesions)
            - deficits in line bisection and crossing, drawing
            - types
                - personal
                - extrapersonal space
                - mental representation
            - also possible to develop extinction=left space neglected if presented together with something on the right
            - pseudo-neglect=tendency to display a reliable leftward perceptual bias during visuospatial tasks in healthy individuals→ evidence of right dominance
                - NB! Phenomenon with reliability issues: with attention-demanding tasks, pseudo-neglect for the left hemi-space (like patients), stronger effect in children and elderly people when compared to healthy adults

- Corbetta & Shulman: hypothesised two networks for spatial attention
  - dorsal fronto-parietal network (FEF-IPS/SPL, top-down orienting of spatial attention)
    - bilateral, no asymmetry
    - endogenous attention shifts
  - ventral fronto-parietal network (VFC-TPJ=bottom-up detection of salient stimuli, ex automatic orientation for unexpected stimuli)
    - right asymmetry
    - ventral frontoparietal network and relationship with regions of damage in patients with unilateral neglect

- Monitoring=checking the (increasing) conditional probability of target occurrence with passing time to optimise behaviour→ right lateral PFC
  - continuous and tonic process
  - implicit temporal preparation=capacity to prepare to give a response for a stimulus→ when it's going to appear, not what or where
    - as a function of passing time, the confidence in an event becomes stronger and the reaction to said event is prepared in advance (ex red light turning green)
  - foreperiod paradigm (Woodrow)=warning stimulus (neutral=it doesn't tell us when it's going to appear) followed by the target stimulus
    - foreperiod=time from warning to target, can be fixed or variable, causing opposite effects on behaviour
    - as time passes by, the monitoring capacity is able to evaluate passing time and the increasing conditional probability that the stimulus will occur now as it has not in the past moments
      - hazard function
      - fixed: short FP=quick answer, long FP=slow
        - Weber-Fechner law
      - variable: short FP=slow answer, long FP=quick
        - hazard function




  - causally linked with right lateral prefrontal regions: if you damage that region, the monitoring does not happen (no effect on variable long trials), replicated with TMS and fMRI in healthy control, especially in the lPFC, whose activity correlates with this effect
  - tested for domain specificity against language (left-lateralized)
    - PET study:
      - verbal tasks (semantic comparison vs phonemic comparison, both strongly left-lateralized) on words clearly pronounced vs degraded (noise)
      - strong activation of the right PFC for degraded material→ monitoring
    - Fleck: dorsolateral prefrontal cortex activated by monitoring different domains under low confidence
      - verbal episodic memory (is the word old or new?) vs visual perception task (is the green area > than the orange surface?)+ confidence rating (1-4)

    - prominent right dorsolateral PFC activation in both tasks, which negatively correlated with the confidence ratings
        - lower confidence=more activation, independent from type of material
        - monitoring a weak memory trace or perceptual evidence
    - also ACC is activated and is correlated with RTs: probably linked to difficulty of the task (as the right PFC activation did not correlate with RTs)

## Mixed asymmetries

Episodic memory has a lateralisation of subcomponents→ HERA Model (Tulving)=Hemispheric Encoding Retrieval Asymmetry→ can be generalised to working memory= capacity to elaborate info temporarily in mind

- Left PFC: encoding new memories (especially verbal material) →
    - semantic processing or strategic organisation of the material to remember, to build up the "response space"
    - processes
- Right PFC: retrieval→ monitors weak memory traces to optimise behaviour
    - familiarity feeling, not pure recollection→ source memory to vouch info
    - could also monitor visuo-spatial decision making on ambiguous stimuli or for low confidence on answers

Motor inhibition→ Inhibition model (Aron)

- Network of three areas interconnected through white matter tracts
    - subthalamic nucleus
    - presupplementary motor area (preSMA)
    - right inferior frontal gyrus
        - → frontal Aslant tract (where?)
    - → other researchers: this network has a more general function -
        - ex IPFC also involved in the VAN: in a stop and answer task promotes inhibition, but in other tasks may cause an answer→ probably detects behaviorally relevant stimuli
- Tasks: stop signal task
- capacity to detect salient and potentially meaningful stimuli very quickly and orient attention

Executive functioning→ ROBBIA model

- Inspired by HERA, but also uses data from patients
- Two main lateralized functions

    - criterion setting=flexible process to set up and select rules, association and inhibition of reactions, association between stimuli and responses, repression of irrelevant info and useless responses, refreshing of necessary info
        - proactive=cue-related
        - lateralized in left fronto-parietal areas
        - phasic activation, in the learning phase→ trial-by-trial manipulation
    - monitoring of task rules
        - quality check on info and performance and correction if needed
        - lateralized in a right fronto-parietal network
        - tonic activation=vigilance, sustained attention
- Evidence
    - left lateralization in PFC
        - verbal episodic memory encoding
        - colour-word Stroop task
        - verbal fluency tasks
        - verbal random number generation
        - → is the left lateralization due to the verbal material or to specific executive processes?
    - Vallesi (2012): visual perception task: speed-accuracy trade off→ non-visual task but studies criterion setting
        - are there more green or orange pixels?
        - cued to priority accurate or quick strategy: constantly switching strategy
        - diffusion model: combines together the distribution of responses for correct and incorrect trials to analyse the performance=how the decision process is going
            - race between correct/incorrect responses
            - if you're quick, you may be prone to errors; if you're slow and get perceptual evidence before answering, there's less possibility for random fluctuation
            - by increasing the distance, you're slower but more accurate; by minimising it you're quicker but make error
            - parameter A="distance"
        - activation of left PFC was correlated positively with parameter A, especially in switching conditions (from speed to accuracy) before you are actually performance the task, during the cue phase=preparing an hypothetical response strategy
            - left PFC: accumulation of perceptual evidence for decision-making
            - maximum activation of left PFC at cue-moment=strategy setting
    - neuropsychological study:
        - left frontal patients adopt a response criterion which is too permissive when they have to change response strategy from quick to accurate
        - VLSM technique to identify brain areas critically involved in criterion setting: left ventrolateral PFC
    - fMRI study of inductive reasoning (Babcock&Vallesi): manipulates the domain by using different tasks, inductive reasoning

- on a screen, random letters in random positions
  - verbal task=do the letters form a word? From which semantic category?
  - spatial task=Does a geometric shape emerge from the position of the letters?
  - control condition=one-back task in both spatial and verbal condition, to exclude areas linked to working memory
- results
  - verbal patterns: activation of left PFC
  - spatial patterns: bilateral activation of a prefrontal area + left cerebellar activation
  - conjunction analysis of both tasks: activation of the left PFC for criterion setting
    - verbal criterion setting vs verbal control
    - spatial criterion setting vs spatial control
    - ventrolateral prefrontal region in the left hemisphere is activated when criterion setting is required, independently on the domain (verbal or spatial)

- Langdon:
  - LH lesions: verbal reasoning deficit
  - LH&RH lesions: spatial reasoning deficits
  - → lesions to left prefrontal cortex cause reasoning deficits (it doesn't matter the type, if spatial or verbal)
    - reasoning is located in the left PFC
    - left prefrontal cortex is involved in reasoning tasks, independently of task domain

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- fMRI of task-switching (Vallesi, Arbula)
  - task cue: word colour, but changing rule
    - spatial
      - roll=clockwise or counterclockwise rotation
      - pitch=forward or backward rotation
    - verbal
      - gender
      - status
  - conditions
    - baseline=1 task per block
    - repeat=same task as previous, slower RT and more errors than baseline
    - switch=different task from previous=slower RT, more errors than repeat
    - → insertional assumption, mixing cost=sustained attention to keep both rules active, even if you need the same one
  - results
    - cost in accuracy and times for switching
    - fMRI: activation in left frontoparietal region for verbal pattern, in spatial pattern frontoparietal activation on the left side and frontal activation on the right side
    - conjunction analysis: clear activations in left frontoparietal regions for criterion setting

        - the laterality index shows that spatial contrast is located in a right fronto-parietal network, whereas verbal contrast is located in a left fronto-parietal network which involves a more ventral region in the left PFC→ representation of domain specific info
        - specific patterns of connectivity can show some degree of lateralization: ex integrity of the fronto-occipital fasciculus predicts perception of faces on the right and verbal capacity on the left
            - criterion setting for rule discovery and task-switching is left lateralized in frontal and fronto-parietal regions
    - which voxels were more activated?→ looking for asymmetries
        - normalisation=each single individual brain is matched to a template=the two hemispheres are the same
        - spatial contrast: on the right side, more activated
        - verbal contrast: on the left side, more frontoparietal activation
            - but frontal activation is inferior
- domain-specific areas in inferior prefrontal regions

- summary on functional hemispheric asymmetries
    - Language
        - Left lateralized? Classical neuropsychological cases (e.g., Broca, Wernicke)
        - But: some language aspects are more right-lateralized (prosody, emotional content)
    - Motor & Action control
        - Left hem. dominance (handedness, apraxia)
    - Spatial attention
        - Right dominance in ventral frontoparietal attentional network (see neglect)
    - Verbal Episodic Memory (HERA model)
        - Encoding: left frontal; Retrieval: right frontal
    - Executive functions (ROBBIA model)
        - Criterion-setting: left; Monitoring: right

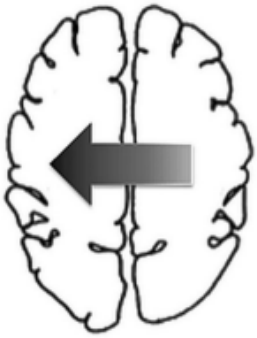
## Models of inter-hemispheric dynamics

- More likely, there's no absolute hemispheric dominance (ex through reciprocal inhibition), but division of labour across the two hemispheres
    - no clear dichotomy, major vs minor hemisphere, no totally lateralized processes
    - all the models presented before show some theoretical or empirical problems

- the hemispheres are more interactive: each occupying functions not taken by the other, usually both are involved in the same function, to a different extent, especially for complex tasks
  - transform themselves toward complementary elements

- Models of inter-hemispheric dynamics
  - insulation: corpus callosum acts as a barrier to prevent interference between hemispheres→ allows separate computations through callosal shielding

    - tested: upright vs inverted letters, for bilateral presentation advantage if upright and inverted letters are in different hemi-fields, but not when they were mixed across fields
      - hemisphere insulation reduces interference
      - when the conflicting tasks were separated (two corners), general advantage of bilateral for division of labour
      - no advantage when they were mixed interhemispherically
  - inhibition: stimulation of one hemisphere suppresses activity in the other
    - stimulus-driven activity in one hemisphere inhibits the homologous regions in the other→ attempt to preserve attentional resources, focusing on just one stimulus in one hemi-field
      - evidence from patients: for a strongly lateralized lesion, disinhibition of the homologous region



    - test: quickly read columns of letters presented in the same vs in different hemi-fields (unilaterally on L, unilaterally on R, bilaterally but first report L and then R, bilaterally but first R and then L) and report as many as possible, attention focused on one side→ conflict between hemispheres, in bilateral presentations no attention to the unrequested side (extinction, iconic sensory memory)
      - very high capacity, very short lasting
    - PET: more metabolic activity in spatio-topic visual cortex where no stimuli is presented (unilateral condition) than when it is presented but not prioritised (bilateral condition)
      - cross-hemispheric inhibition view: in bilateral stimulation reduced activity in regions contralateral to the unrequested hemi-field (unilateral trial > bilateral trial)
  - Cooperation: the hemispheres collaborate in complex tasks
    - when computational demands are high, collaboration is more beneficial than isolated processing

    - evidence: as task complexity increases, cross-hemisphere conditions produce better performances than within-hemisphere conditions
      - name-identity task: press the button if the bottom item had the same name as any of the top items and refrain from pressing if it did not (go/no-go, complexity manipulated by increasing the number of items to compare + to keep the fovea in the middle and prevent attentional effects, name the number in the middle)
        - when items are presented in different hemi-fields, advantage through communication between hemispheres (parallel processing across more units)
        - when task demands and an individual's asymmetric hemispheric activation both load on the same

hemisphere, the ability to divide the processing between the hemispheres is limited
        - NB! Interhemispheric division of processing allows a better performance for more complex tasks only if required operations can be divided between hemispheres. In the same way, cross hemispheric processing would only be a cost for simple tasks (time-consuming), whereas within-hemisphere processing would yield satisfactory results
    - interpretations
        - under high task demands: info could be spread across a larger number of processing units in both hemispheres
        - cooperation allows processing in parallel
        - for simple tasks, is counterproductive

Testing hemispheric preference

- Chimeric face test=combination of a neutral and happy/sad face→ which one expresses more happiness/sadness?
    - (n. of pairs with right attentional bias- n. of pairs with left attentional)/total n. of pairs
    - hemispheric asymmetries in expression and recognition of emotions
    - in studies involving chimeric faces, emotional expressions are perceived as more emotional when presented in the left visual field (right hemisphere)
    - the two halves of the brain are believed to play different roles in emotional processes
- Approach/withdrawal motivational model of the PFC (Davidson, 1998)=left PFC mediates approach motivation and behaviour vs right PFC withdrawal motivation and behaviour
    - two motivational systems closely connected with emotions, viewed as action dispositions or motivationally tuned states of readiness
    - affective disposition=balance between the two motivational systems, if imbalanced it is possible to develop psychiatric conditions
        - more right activation in depression: for left frontal lesions, patients are usually more depressed (NB! May be an effect of more evident deficits)
            - appetitive motivation approach is smaller, defensive motivation withdrawal is bigger
            - in EEG studies depressed patients showed an asymmetry in alpha waves: more alpha in the left PFC=less active
            - in other cognitive tasks in which depressed patients showed less/more interference from specific material
        - NB! It is a tract rather than an acute marker, it is present also in patients in remission
        - NB! Effect modulated by many factors (age, gender)

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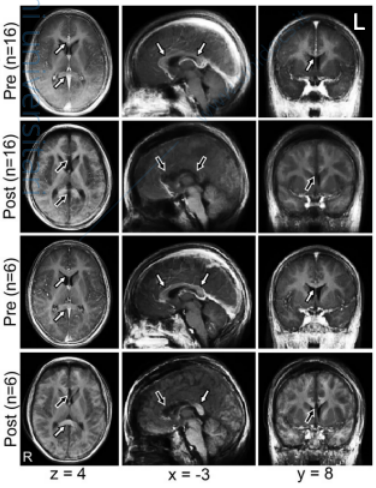
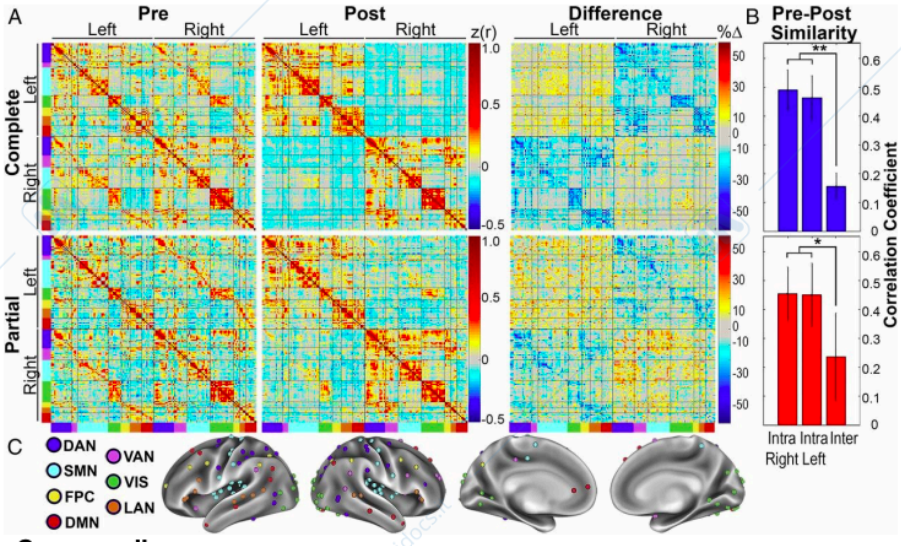
## Split brain models

- Sperry: commissurotomies to treat generalised drug-resistant epilepsy
    - each hemisphere hosts its independent stream of conscious awareness and has its own separate chain of memories and representations, inaccessible to the other hemisphere
        - ex right dominance for visuospatial tasks: in a block-test the right hand is incapable of completing the task on its own, whereas the left hand executes the task perfectly
- Gazzaniga: studying split-brain patients gives the opportunity to discover how the two hemispheres work independently and how this affects the conscious perception of the patient
    - WJ (Block test): right hand (LH) incapable of matching a set of blocks to a pattern on a card, left hand (RH) execute the visuo-constructive task well
    - studies on the LH interpreter: mono-hemispherical presentation of images, then each hand chooses an image according to what it sees
        - when the patient is asked about the image chosen by the left hand, the left hemisphere (= language) invents a logical explanation by interpreting the context and
            - reflection on frailty of awareness/consciousness=not a unitary phenomenon as we think, it's a matter of interpretation→ sometimes a posteriori (post-hoc) explanation even with non-split brain
                - anosognosia
    - recent studies on split-brain models shifted the focus on structural and functional connectivity in an effort to understand the hemispheres and their communication
        - Roland, 2017: MRI and fMRI before and after a complete vs partial callosotomy→ resting-state fMRI results showed that only interhemispheric connectivity (vs intrahemispheric) was damaged by the callosotomy, with some connectivity preserved in the partial cut
        - Voxel Mirrored Homotopic Connectivity analysis (VMHC, measures synchrony in activity with homologous voxels=strong index of interhemispheric connectivity): for a complete callosotomy distribution centred around 0, whereas for partial cuts still some homotopic



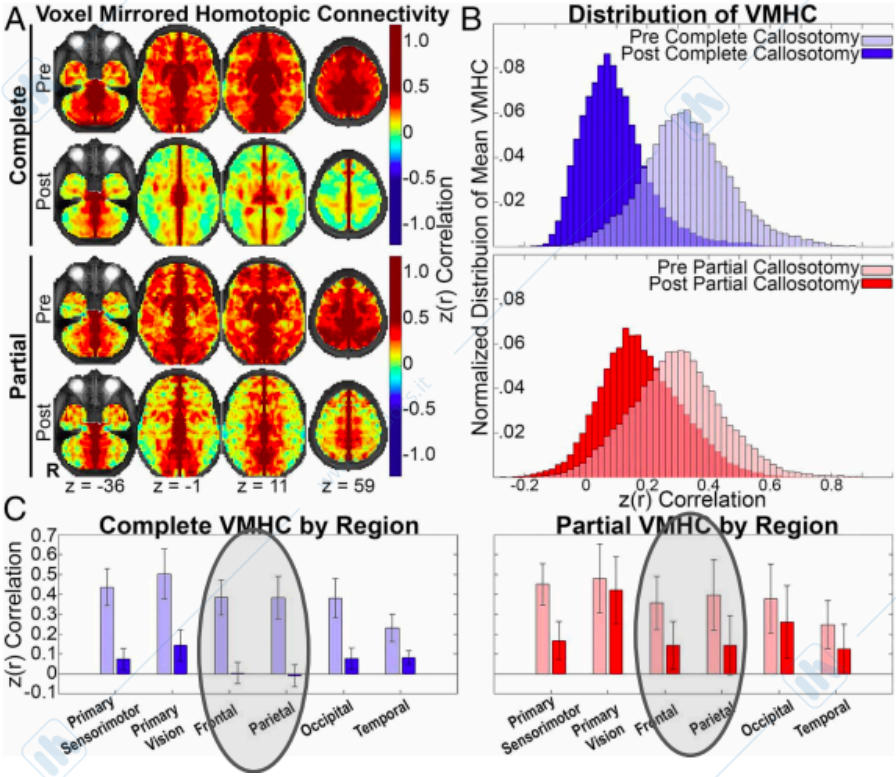
connectivity preserved (distribution shifted from 0)




- lost connectivity between hemispheres, especially for complete callosotomy
    - corpus callosum=causal role in maintaining functional connectivity between hemispheres
- MHC analysis divided by regions shows that some homotopic connectivity is still preserved in some areas even after a complete callosotomy
    - presence of other commissural tracts, especially for primary areas: less dependent on the CC than associative regions, other regions besides the CC might connect these homologous regions
- invasive tracing: relatively sparse axonal connectivity via the CC in the hand area of M1 (callosal holes) has been found. Callosal connections between V1 are also very sparse => likely contribution of subcortical structures of resting-state cortical network connectivity
    - after a partial commissurotomy (which usually involves the rostral part of the CC), some frontal homotopic connectivity is still present
        - posterior parietal-occipital connections (splenium) can adapt to support frontal homotopic functional connectivity, probably via intra-hemispheric white matter connections (e.g. superior longitudinal fasciculus)
        - no disconnection syndrome is usually observed after partial callosotomy preserving the splenium
- frontal and parietal regions, after complete callosotomy, almost completely lost voxel mirror connectivity
    - in partial callosotomy connectivity remains: connectivity could occur bypassing the rostral part of corpus

callosum; you can keep some residual connectivity through interhemispheric connectivity as splenium

- preserved homotopic FC following complete callosotomy in primary areas



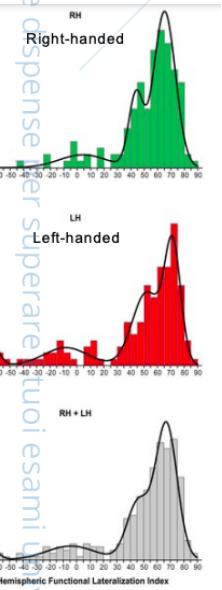

- other regions besides from corpus callosum might connect these homologous regions
- subcortical contribution of resting-state cortical network connectivity
- Preserved homotopic FC following complete callosotomy in primary areas
- polysynaptic FC after partial callosotomy
- Homotopic FC in prefrontal cortex is less reduced after partial vs. complete callosotomy, BUT callosal fibres connecting these areas are sectioned in both procedures! àPosterior parietal-occipital connections (spared splenium) can support frontal homotopic functional connectivity - Probably via intra-hemispheric white matter connections (e.g., superior longitudinal fasciculus) - Explains why no disconnection syndrome is usually observed for partial callosotomy sparing splenium (Gordon et al., Brain, 1971)

- NB! CC disconnection syndromes are actually quite rare: usually the behaviour of split-brain patients is subtly changing
  - no clear-cut distinction between left and right hemisphere functions→ the hemispheres work together to optimise functions, plasticity helps recover through alternative patterns
    - anterior and posterior commission, fornix

- theory of left hemisphere as logic and right hemisphere=creativity is quite popular in the general public
    - over-simplified, to such a point that it becomes incorrect -> “for most cognitive activities, you actually need both hemispheres” (Gross)

Are brain functions lateralized together in the same individual? Ex left-handedness is also right-lateralized for language?

- fMRI study (Mazoyer, 2014): probability maps produced from activation signals during sentence generation (vs repetition of overlearned lists) by right-handed people show a significant left lateralization in most subjects, with just a few of them being actually right-lateralized or bilateral
    - the distribution for left-handed people is very similar but with more variability→ 5% of subjects show right lateralization or bilateral language
    - the distribution of the whole population shows mostly left-lateralized language, with some variability
    - NB! A different lateralization of language is not problematic for normal functioning, but it’s relevant when it comes to surgery (to spare it) and lesions
        - crossed aphasia=caused by a right lesion in a right-handed patient. Language can be localised through fMRI or TMS (not invasive), previous to their development the Wada Test was used




- Probability map of right-handed participants having a significant activation during sentence generation for language
    - some left-handed are strongly right-lateralized for language as well, but most right-handed are left lateralized ??????
    - bigger dispersion in the left-handed than in the right-handed, for language
    - at the population level
        - Most right-handers (green) are extremely left lateralized for language
        - Most left-handers (red) are also left lateralized for language, although some are right lateralized

Possible evolutionary advantages of functional hemispheric specialisation

- In evolution, there are no cause-effect relationships because changes happen in the long period and it’s impossible to control all the variables involved
- Maybe the richness and heterogeneity of human mind capacities could have requested dedicated neural circuits, with specialised computations for each high-level cognitive and emotional functions in either hemisphere
    - Corballis: cerebral asymmetries are an advantage to minimise redundancy and conflict: having a doubled neural substrate for a function is a waste of space and resources, the specialisation of hemispheres may be computationally convenient
        - the complementary specialisation of the hemispheres can be computationally more efficient

        - evidence: deviations from the typical cerebral dominance pattern is associated with a series of disturbances such as stuttering, dyslexia, or increased risk of schizophrenia
            - correlational data for mixed handedness=higher risk of schizophrenia
            - in most animals lateralization is distributed at random, but in humans functions are clearly lateralized in the population
    - Possible evolutionary advantage of the minority with opposite lateralization (left-handed): “surprise effect” that can be an advantage in a fight
        - left-handed basketball players have better performance averages and significantly longer careers than right-handed ones. In hockey, mixed handedness brings an advantage to players