# THE PLASTIC HUMAN BRAIN

* With **Hebbian Plasticity** we refer to the theory by *Donald Hebb* according to which ***repetitive activation of neuronal circuits*** can induce ***long-term changes in subsequent responses generated by synapses in many regions of the brain***
* such plasticity of synaptic connections is regarded as a cellular basis for developmental and learning-related changes in the central nervous system, namely persistent activities tend to induce lasting ***cellular changes in order to increase its stability whenever the activity is repeated again***
* a certain stimulus can trigger a response in a particular area of the brain; repetitive activation of this neuronal circuit will improve the used connections in the region, making the overall response faster and easier to a said stimulus.
* e.g. when an axon of cell *A* is near enough to excite a cell *B* and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that *A*'s efficiency, as one of the cells firing *B*, is increased
* namely, every time *A* successfully excites *B*, it is like their connection gets strengthened so that, the next time, there response will be faster
* evidences of this theory have been found in macaques and humans, in particular with respect to the role of *feedback projections* from secondary to primary visual areas in visual awareness as well as the state of the primary visual cortex itself
* ******e.g. ***visual motion perception tasks***, namely *tasks in which subjects have to detect the direction of the motion of certain objects or group of objects*, are particularly related to the state of *V1* and to the feedback projections coming from *V5* (motion visual area) to *V1*
* indeed, the brain processes motion by comparing the state of a group of neurons with the state of the same group of neurons in the previous “time unit” and, thus, checking if and how this state has changed
* ***Digression: two-way traffic in the brain – feedback and forward pathways in visual processing***
* **Visual processing** is a term that is used to refer to the brain's ability to use and interpret visual information from the world around us. The process of converting light energy into a meaningful image is a complex process that is facilitated by numerous brain structures and higher-level cognitive processes. (vedi Lesson 4 schema)
* The visual system is organized hierarchically, with anatomical areas that have specialized functions in visual processing.
  + **Low - level visual processing:** is concerned with determining different types of contrast among images projected onto the retina (It includes the simply detection of something in the external environment)
  + **High - level visual processing:** refers to the cognitive processes that integrate information from a variety of sources into the visual information that is represented in one's consciousness. (It includes object recognition, object location…)
* High-level visual processing depends both on top-down and bottom-up processes.
  + **Bottom-up processing** refers to the visual system's ability to use the incoming visual information, flowing in a unidirectional path from the retina to higher cortical areas
  + **Top-down processing**refers to the *use of prior knowledge* and context to process visual information and change the information conveyed by neurons, altering the way they are tuned to a stimulus
    - All areas of the visual pathway except for the retina are able to be influenced by top-down processing.
* Traditional view of visual processing, bidirectional visual pathways:
  + **Feedforward system**: one-way process by which light is sent from the retina to higher cortical areas (bottom-up process).
    - In visual context the low-level visual processing is the understanding of basic image features like orientation and contrast. This information is passed to higher-level areas through feedforward.
  + **Feedback system:**  top-down process
    - In visual context, higher level areas use the information coming from the feedforward process, to detect more complex image aspects; this complex information is then shared with the lower areas through feedback connections.

Information from lower areas is transmitted truthfully to higher level areas, whereas information that is sent back from higher areas to the lower areas strongly depends on the interpretation of the visual world.

* **Connectivity: how visual motoion areas are connected?** 
  + Feedforward from V1 to V5, feedback from V5 to V1.
* In the **following experiments** will be shown that we can achieve better performances in visual motion perception, by stimulating the feedback process from V5 to V1. (We know that V1 is the visual area related to the low-level processing, while V5 is the visual area related to visual motion – higher level information related to the orientation and direction of the input stimulus).
  + Depending on the complexity of the motion we will have a complex pattern brain activation.

EXPERIMENT 11***: Empowering Re-entrant Projections from V5 to V1 Boosts Sensitivity to Motion, Romei, Chiappini, Hibbard, Avenanti, 2016***

* The aim of this experiment was to causally test ***how the feedback connectivity from motion visual area (V5) to V1 affects sensitivity to motion*** (we should see an anhancement of the connectivity) by ***directly modulating this connectivity*** using a novel *ccPAS* paradigm
* ***ccPAS***, namely *cortico-cortical paired associative stimulation*, is a paradigm in which two *TMS* pulses are fired in two different areas of the brain, possibly with a delay with the two pulses
  + These to pulses of TMS are applied one over V1 and one over V5 repeatedly, to emulate Hebbian Plasticity.
  + We are not stimulating just a pre-synaptic neuron and a post – synaptic neuron, but we are stimulationg a neuronal population made of a big number of neurons.
* The experiment want to demonstrate that if we are able to interfere with the feedback connection from V5 to V1, we can create a new state of the cells (hebbian plasticity of the brain) in a way that in new trials of this visual-motion observation we can achieve better results because we have developed a sort of background knowledge. (my opinion)
* The *32* participants of the experiment were split in *four groups* and, while recording their brain activity through *EEG*, they were undergone a *visual motion perception stimulus* (both in the right hemifield and in the left one with the same probability) in which particles were moving either left or right
* at first, the motion coherence of the particles was specifically calibrated so that each participant would guess the right answer about *75%* of the times

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* then, each group was subjected to a different kind of stimulations, each one changing one parameter so to have meaningful control data
* in the *experimental group*, named, *90 paired pulses* were given in *V5* at first and in *V1* later with a delay of *20ms*, where *20ms* is on average the time that it takes a stimulus in *V5* to reach *V1* (time taken by the signal to go from the presynaptic activating in V5 to the post synaptic target in V1)
* in the *direction control group*, named , the same pulses were given in *V1* at first and then in *V5* in order to show a correlation with the direction of propagation of the stimulus in the brain (so to show that we can have better result following/stimulating the feedback path, not the feedforward path)
* in the *timing control group*, named , the same pulses were given in *V1* and *V5* at the same time in order to show a correlation with the duration of propagation of the stimulus in the brain (so to show that we need to respect the biological time of the delivery of the signal from V5 to V1; if we delete this timing we may lose the Hebbian plasticity effect)
* in the *placebo control group*, named , the same pulses were given from *V5* to *V1* with *20ms* delay but using a *sham TMS* (no TMS is actually applied)
* after a demo session in which subjects were trained to respond to the task and a ***baseline session*** to measure the accuracy prior to the stimulation, it followed the *ccPAS* stimulation and, eventually, other ***four sessions***, respectively after *0, 30, 60* and *90 minutes* from the stimulation, in which the accuracy of subjects was measured

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* in practice, the aim of the *ccPAS* session is to increase the connectivity between neurons in *V5* and neurons in *V1* by simulating a fake propagation of the potential from *V5* to *V1*, namely to simulate the training of neurons in *V5* to have a higher sensitivity with respect to motion perception tasks in order to increase the performance of members of the experimental group
* results shown that *only members of the experimental group* exhibited an improvement in the motion perception task (expressed in terms of Δ percentage of coherent motion correctly guessed *75%* of the times) particularly *30* and *60* minutes after *ccPAS*, while the effect was started reducing after *90* minutes



* this can be seen as the proof that applying *ccPAS* ***over two functionally connected visual regions improves visual processing depending on the parameters of stimulation*** (e.g. directionality, specific timing, …), and that ***empowering reentrant connections from V5 to V1 implicated in the conscious perception of visual motion boosts visual motion sensitivity***
* Results provide ***first causal evidence*** that selective empowering of reentrant projections from V5 to V1 can enhance visual processing of motion.

EXPERIMENT 12***: Strengthening functionally specific neural pathways with transcranial brain stimulation,*** ***Chiappini, Silvanto, Hibbard, Avenanti, Romei, 2018***

* Similarly to the previous experiment, this one aimed at directly modulating this connectivity using the *ccPAS* paradigm, still, in this case, the *ccPAS* stimulation was performed at a peri-threshold intensity while participants were made to see the a stimulus itself with particles going *100%* either towards the left or towards the right in order to ***strengthen just the specific neural pathway coding for that specific direction***
  + So we are looking at whether the participants could get better at a particular unit of network, assuming that we are looking at a system capable of predicting all sensing motion only in one specific direction.
* At first, a *phosphene threshold assessment*was carried out on each of the *16* participants in order to find the correct *ccPAS* *intensity*, then these participants were split in *three groups* and the procedure repeated for three sessions in three different days
* each group was subjected to a different kind of stimulations, each one changing one parameter so to have meaningful control data (1 experimental condition and 2 control conditions)
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  Descrizione generata automaticamentein the *experimental group*, named, *90 paired pulses* were given in *V5* and then in *V1* with *20ms* of delay at an intensity in the amount of *80%* of the previously measured phosphene threshold
  + V5 was not stimulated at a fixed intensity, but at an intensity below the phosphene threshold, in order to not induce a particularly activity in the brain, but activating only those neurons that were coding for this movement.
* in the *intensity control group*, named , the same pulses were given at an intensity in the amount of *100%* of the phosphene threshold in order to show that the effectiveness of the stimulation is correlated with a precise and localized activation of certain neurons
* in the *direction control group*, named , the same pulses were given at first in *V1* and then in *V5* in order to show a correlation with the direction of propagation of the stimulus in the brain
* eventually, *30* minutes after the stimulation, participants were subjected to the *visual motion perception task* and their accuracies both in case the direction was congruent to the one presented during the stimulation or incongruent to that
* Summing up:
  + We went from a phosphene threshold at the beginning for identifying the intensity of stimulation needed to see the phosphene.
  + Then the subject does the motion discrimination task (baseline condition) followed by the ccPAS in the three conditions (done on the same subject in different days).
  + Then we wait 30 minutes for the results in the subject.
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  Descrizione generata automaticamenteresults shown an ***increment in the accuracy only in the experimental group and only in the tasks congruent with the stimulation***
* again, this can be seen as s proof that it is possible to induce neural plasticity through the *ccPAS* protocol and, in particular, that ***this induced neural plasticity can be targeted on specific neural pathways***
* From these (and other studies), we could conclude that
* Functional connections are highly plastic in the brain and follow Hebbian rules, and ***ccPAS can temporarily induce this Hebbian-like plasticity in the visual system*** as well as targeting and enhancing the efficiency of specific pathways which can be functionally selected
* Feedback connectivity allows for efficient processing of information, in particular re-entrant connectivity from higher order to early visual areas is functionally relevant to motion perception
* e.g. ***re-entrant V5-V1 pathways carry function-specific information for the processing of motion direction***
* Cognitive Neuroscience developments have allowed for causal testing of such principles in the human brain

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