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## Plasticity

# Neurofeedback for cognitive enhancement and intervention and brain plasticity



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### ABSTRACT

In recent years, neurofeedback has been used as a cognitive training tool to improve brain functions for clinical or recreational purposes. It is based on providing participants with feedback about their brain activity and training them to control it, initiating directional changes. The overarching hypothesis behind this method is that this control results in an enhancement of the cognitive abilities associated with this brain activity, and triggers specific structural and functional changes in the brain, promoted by learning and neuronal plasticity effects. Here, we review the general methodological principles behind neurofeedback and we describe its behavioural benefits in clinical and experimental contexts. We review the non-specific effects of neurofeedback on the reinforcement learning striato-frontal networks as well as the more specific changes in the cortical networks on which the neurofeedback control is exerted. Last, we analyse the current challenges faces by neurofeedback studies, including the quantification of the temporal dynamics of neurofeedback effects, the generalisation of its behavioural outcomes to everyday life situations, the design of appropriate controls to disambiguate placebo from true neurofeedback effects and the development of more advanced cortical signal processing to achieve a finer-grained real-time modelling of cognitive functions.

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## 1. Introduction

While neuronal plasticity culminates during foetal and post-natal early life, and continues into childhood and adolescence, the human brain is able to learn and adapt to an ever moving environment all throughout life, including into adulthood and older age. This is made possible thanks to specific neuronal

and network brain mechanisms that reshape brain functions. Generally speaking, brain plasticity consists in brain structural reorganisations such as changes in white matter myelination or grey matter volume, correlating with functional reorganisations involving the creation of novel synaptic connections and the reinforcement or weakening of existent synapses. Although plasticity is higher before adolescence, especially

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during brain developmental windows known as critical periods, neuronal plasticity is retained all throughout life. Plasticity is thus the basis of brain development and learning. It can be stimulated by cognitively demanding activities such as reading, music, arts, sports, studies, etc. Brain ability to learn new contingencies can further be stimulated or enhanced relative to more classical approaches, including in clinical environments, thanks to specific trainings involving the repeated execution of precisely designed behavioural protocols. These behavioural protocols often derive from laboratory environments, and their usability in open environments is often increased by imbedding them in playful resources including so-called serious games. A sub-family of these behavioural protocols combine behavioural training with a directed control on physiological signatures, such as heart rate (biofeedback) or cortically generated signals (neurofeedback), in real-time, such that the participants can learn to associate this feedback with the behaviour they are producing. In particular, neurofeedback is a method based on providing to the participants, whether patients or healthy volunteers, information about their brain functions during the production of a given behaviour (Fig. 1). This information that is fed back to the participant can be a direct level of activation of a specific brain region causally involved in the behaviour of interest, or more refined information reflecting more specific brain functions, such as a functional connectivity measure or a decoded brain state or cognitive information. Neurofeedback has been shown to trigger positive behavioural outcomes such as relieving advert symptoms or improving specific cognitive functions. These positive behavioural outcomes rely on brain plasticity mechanisms and the ability of subjects to learn all throughout life. Neurofeedback is thus considered as a

powerful method to trigger brain plasticity, by initiating specific functionally relevant changes in the brain such as changes in white and grey matter microscale properties, or changes (increase or weakening) of functional connectivity. Here, we review the main approaches implemented to perform neurofeedback and we discuss their behavioural outcomes on healthy or impaired participants. In addition, we describe the different effects of neurofeedback on brain plasticity, possibly supporting the observed behavioural improvements. Last, we discuss the limits of neurofeedback in terms of transfer learning and generalisation of behavioural benefits to everyday life environments, the duration of behavioural and brain effects as well as methodological limits associated with this type of studies (Fig. 1).

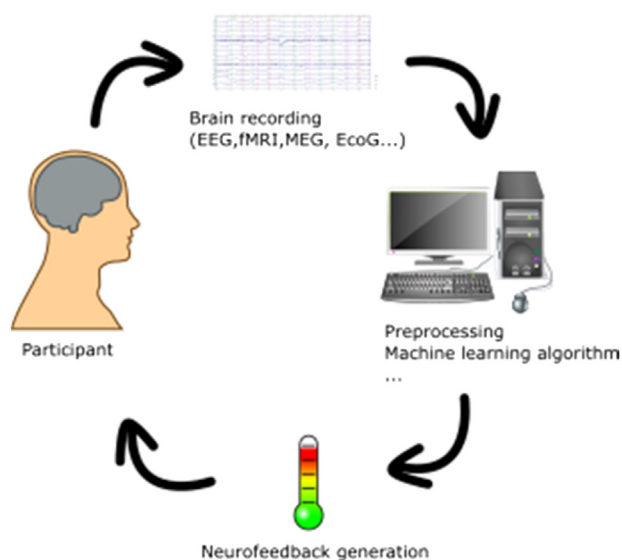
## 2. Principles of neurofeedback

Neurofeedback is a tool which is based on recording the brain activity of the participant, and providing him/her with a feedback on this brain activity, in real-time [1,2]. The main assumption of this approach is two-fold:

- a direct action on the activity of a specific brain region can have observable and controllable effects on behaviour; and
- cognition can be enhanced by the subject him/herself, by a direct control over his/her internal brain computations, provided he/she is given access to them in real-time.

Brain activity is fed back to the subject in multiple ways. For example, the participant can hear his/her brain activity (or an informational quantification of this brain activity), brain signal intensity being directly translated into auditory signal intensity. Elsewise, the participant can be shown his/her brain activity as a virtual reality ball approaching or moving away from a target, a disc changing in size, or a gauge filling up at varying speed. Task difficulty can also be manipulated, such that the task becomes more (or less) difficult as a function of a quantification of brain information during the trial. All these types of neurofeedbacks have as effect to establish an explicit (sound, ball) or implicit (task difficulty) relationship between the participants' brain activity and task events.

Most often, driving signals for non-invasive neurofeedback approaches are based on electroencephalogram (EEG), electrocorticogram (ECoG), magnetoencephalography (MEG) or functional magnetic resonance imaging (fMRI) recordings [3,4]. The initial neurofeedback developments provide the participants with information about raw brain activity. For example, in fMRI-based neurofeedback, participants are provided with a feedback on their raw blood oxygen-level dependent (BOLD) activity in a brain region-of-interest (ROI), relative to a reference epoch in the task. In most cases, subjects are asked to implicitly increase or decrease the level of BOLD activation in this ROI by increasing or decreasing the size of a disk or the height of a gauge [5]. In EEG-based neurofeedback, participants are typically presented with pre-processed EEG recordings, such as the oscillatory power of EEG signals in specific functional frequency bands such as the alpha, gamma, or beta bands [6]. In fMRI or MEG based neurofeedback, functional connectivity metrics between task-related cortical regions can



**Fig. 1 – Schematic representation of neurofeedback experimental designs. Brain activity is recorded while participants are performing a specific behavioural task. This activity is processed in real time. The outcome of this processing is fed back to the participants, for example as a gauge. Participants are instructed to manipulate gauge level by controlling their brain activity.**

be used as a feedback [7]. Again, in these procedures, a visual feedback is often provided, with a size or a height representing the neurofeedback metric. The participants have to work on increasing or decreasing this visual feedback, and as a correlate, they have to actively (though not necessarily consciously) control the level of the brain generated metric on which the neurofeedback is based. Using raw or minimally transformed signals has the advantage of being easy to implement with only few (and fast) processing steps (Fig. 2). EEG event-related potentials (ERPs) can also be used to provide neurofeedback as seen in protocols using the P300 speller or its several variants [8]. In this type of approach, selective attention can be targeted by training the participants to enhance the attention-related modulation of visual ERPs, under the strong hypothesis that this is going to impact general attentional processes beyond this specific task [9].

A major disadvantage of these approaches is that the feedback provided is based on raw signals and thus lacks

functional specificity. In order to generate informationally more precise/accurate/specific feedbacks, advanced neuronal information processing methods can be used. In particular, advances in machine learning methods allow to infer the participant's brain control signals in a more informative way. For example, in 2012, EcoG recordings were used to infer precise motor commands in a tetraplegic patient, thus allowing this patient to control a robotic arm [10]. This type of approach is considered as highly informative, as the patient was able to control multiple degrees of freedom of the robotic arm. Likewise, in fMRI, decoding of scene- versus face-related brain activations has been used as a neurofeedback on higher order attention-driven cognitive functions [11]. Other approaches have yet applied BOLD decoding approaches to access the participant's degree of confidence in his/her performance in the task [12]. These latter decoding approaches can provide more refined information on cortical processes than raw signals, and decoded neurofeedback can be more informative

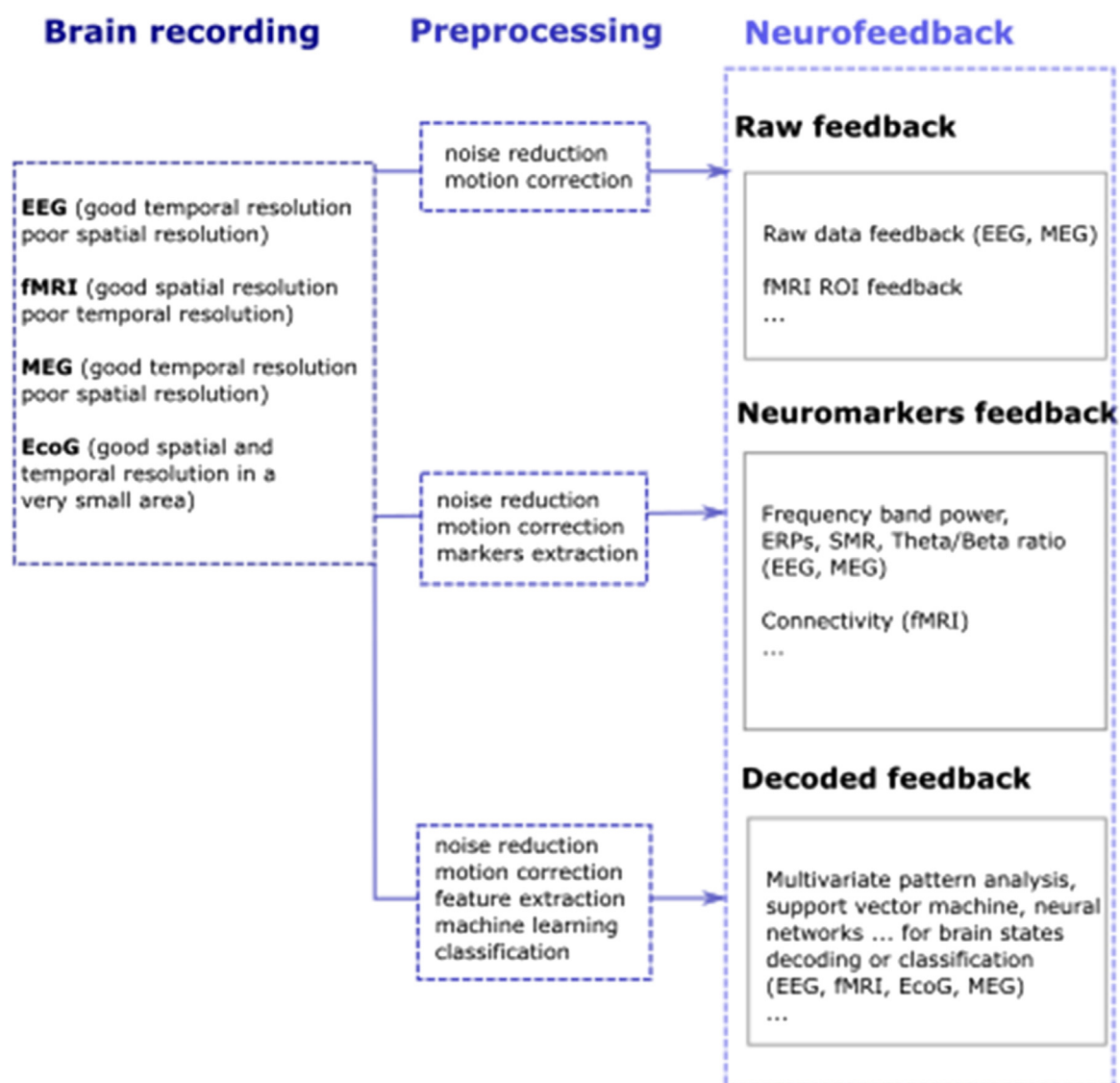


Fig. 2 – Summary of current neurofeedback implementation steps, from initial recorded brain signals, to preprocessing procedures and actual neurofeedback metrics.

about the subject's individual neuronal specificities. For example, in de Bettencourt et al., participants had to focus either on faces or landscapes in images mixing both information items, and feedback was provided based on how the decoder estimated that attention was successfully oriented, in time, on either the faces or the landscapes. Feedback was implemented as an increase or a decrease in the difficulty of the task, thus forcing subjects to refocus when they were not [11]. This decoded neurofeedback (DecNef) method is a powerful tool to provide very fine information to the participants. However, it can be challenging to implement as the pre-processing pipeline can become very complex (Fig. 2).

These latter approaches relying on a complex decoding of neuronal signals in real-time, while highly promising to enhance cognitive functions, are still limited in that they mostly rely on two-category decoding approaches. More recently, Lorient et al. have demonstrated the possibility of precisely tracking spatial attention, in one of eight possible portions of space, in a manner that is highly predictive of behavioural performance [13]. This represents a major advance in the sense that it opens the way for more refined neurofeedback procedures specifically targeting the neuronal computations underlying a given cognitive function. To make this point explicit, the following analogy can be drawn. Brain-machine interfaces (BCIs) allowing subjects to control robotic arms thanks to their brain activities were initially endowed with very coarse spatial control and limited degrees of freedom. More recent generations of motor BCIs approach the capabilities of natural arm movements. At this time, cognitive neurofeedback approaches are still relying on a coarse targeting of cognitive information. Finer-grained access to cognitive information, as in Lorient et al. [13], or as currently implemented with more invasive approaches [14–18], is thus expected to have a dramatic impact on the cognitive effects of neurofeedback.

Neurofeedback can thus be used as a cognitive training tool in order to improve, replace or restore a given cognitive function. It relies on humans' learning abilities and plasticity. In fact, it has been shown that neurofeedback stimulates plasticity by activating well-known reinforcement learning networks [19,20]. The effects of neurofeedback on behaviour and on brain structures are discussed next (Fig. 2).

### 3. Behavioural effects of neurofeedback and clinical applications

Neurofeedback can either be used with therapeutic or rehabilitation objectives, or as a pure cognitive training tool for healthy volunteers (see Table 1 for an overview of selected studies). In the therapeutic domain, neurofeedback has been widely used in order to relieve a wide range of psychiatric disorders such as schizophrenia, addictions, depression, anxiety or post-traumatic stress disorder. For example, neurofeedback based on alpha activity from EEG recordings has been shown to efficiently alleviate depression. This effect is causally correlated with a decrease in global alpha activity in the left hemisphere, which is considered as a biomarker of depression [21]. Likewise, fMRI neurofeedback aiming at

decreasing BOLD activity in the amygdala has resulted in positive clinical outcomes on depression and anxiety. In the context of post-traumatic disorders, EEG-based neurofeedback has been shown to relieve effects on stress, depression and self-harm [22]. Last, EEG- and fMRI-based neurofeedback have shown positive clinical outcomes on addiction symptoms [23]. For example, an fMRI neurofeedback aiming at reducing ventral anterior cingulate cortex activity in nicotine addictive patients has shown a reduction of nicotine use [24] (Table 1).

Neurofeedback has also been used as a neuro-rehabilitation tool to train and restore specific cognitive deficits. The main example of this type of applications is the use of this procedure to enhance attention in attention deficit and hyperactivity disorder (ADHD) patients. ADHD is a disorder which can be treated either by cognitive rehabilitation or by pharmacological treatments such as methylphenidate. While cognitive rehabilitation is not equally efficient in all patients, drugs often come with strong side effects that result in a reluctance of patients or families to rely on such approaches [25]. This has led to the development of a range of specific cognitive neurofeedback-based trainings, compatible with patient care, and with no side effects. ADHD neurofeedback is mainly performed using EEG recordings and using biomarkers such as the theta/beta ratio (TBR), i.e. the ratio between theta and alpha power in EEG recordings, the sensorimotor rhythm (SMR), i.e. the wave which can be recorded on the electrodes close to the sensorimotor cortex, in a 13 to 15 Hz frequency range, and slow cortical potential (SCP), i.e. slow electric shifts (from negative to positive or reversely) during EEG recordings [26]. However, although neurofeedback for ADHD patients is now well-known to provide notable improvements of attention deficit symptoms, its behavioural outcomes, on such indicators as inattention symptoms and hyperactivity and impulsivity symptoms, remain lower than those obtained following pharmacological treatments [25].

Neurofeedback can also be used in healthy patients in order to modify healthy cognitive functions. For example, DecNef using fMRI results in an improvement of visual perception [27], or categorical attention performance [11]. DecNef using fMRI modifies healthy volunteers' self-confidence while performing a discrimination task without changing their discrimination performances [12,28]. fMRI DecNef is also shown to enhance colour perception of an achromatic visual stimulus by training the volunteers on colour perception [29].

These recent studies thus clearly show that neurofeedback leads to behavioural changes in task-specific domains in the short term. However, it is still unclear whether these changes can last during longer periods of time at a distance from the neurofeedback and whether these behavioural changes can be transferred to other tasks than the specific task the participants were trained on during neurofeedback. In fact, very few studies have been able to test the effect of training, weeks or months after the neurofeedback sessions. ADHD neurofeedback shows long-lasting effects of neurofeedback up to 12 months after the last session [30]. Colour neurofeedback on achromatic stimuli shows a sustained effect up to five months [29]. This thus strongly suggests that effects can be long-lasting, confirming the clinical relevance of neurofeedback approaches.



**Table 1 – Non-exhaustive summary of neurofeedback (NF) protocols applied in multiple clinical and experimental conditions, illustrating the variety of trainings, number of subjects, controls procedures and reported effects.**

	Reference	NF Signal	Type of NF	Group size	Control	Short/long term effects	Behavioural and brain induced changes
Depressive disorder	Choi et al., 2011 [61]	EEG	Alpha band activity in right frontal cortex	24	Placebo group	Short: depression relief	
	Linden et al., 2012 [62]	fMRI	BOLD signal in insular cortex and right ventral striatum, and temporo-parietal junctions	8	Control group with cognitive training but no neurofeedback	Short: depression relief	
	(Peeters et al., 2014 [63])	EEG	Alpha asymmetry	9	No	Short: clinical outcomes	
	Young et al., 2014 [64]	fMRI	BOLD signal in amygdala	23	Control group	Short: anxiety relief	
Anxiety, phobic disorder, post traumatic stress	Kopřivová et al., 2013 [65]	EEG	Neurofeedback on first component after independent component analysis	20	Randomized controlled clinical trial with sham neurofeedback	Short: improvement in compulsory behaviour	
	Zilverstand et al., 2015 [66]	fMRI	BOLD signal in dorso lateral prefrontal cortex or insula	18	Single blind randomized control	Short: anxiety reduction	
							Long: effects remain after 3 months
	Kolk et al., 2016 [67]	EEG	Decrease slow (2–6 Hz) and fast (22–36 Hz) oscillatory activity while simultaneously increasing the power spectrum of mid-range (10–13 Hz starting point) activity	52	No but participants have undergone at least 6 months of psychotherapy that can serve as a control for non-neurofeedback training	Short: symptoms reduction	
						Long: effects remain to one month after neurofeedback	
	Chiba et al., 2019 [68]	fMRI	Decoding neurofeedback	4	No but comparison with other methods using EEG and fMRI neurofeedback	Short: fear reduction	
Personality disorder, schizophrenia	Konicar et al., 2021 [69]	EEG	Slow cortical potential	14	No	Short: plasticity changes	Suppression of overrepresentation of slow frequency bands such as delta and theta band activity, after EEG neurofeedback
	Surmeli et al., 2012 [70]	EEG	Neurofeedback based on EEG abnormalities per participant	51	No	Short: clinical improvement	
							Long: clinical improvement after 22 months

Table 1 (Continued)

	Reference	NF Signal	Type of NF	Group size	Control	Short/long term effects	Behavioural and brain induced changes
Addictions	Weiss et al., 2020 [71]	fMRI	BOLD signal on ventral striatum	88	Yes, control group had to modulate activity in auditory cortex	Short: clinical improvement  Long: clinical improvement 3 months after	
	Hanlon et al., 2013 [24]	fMRI	BOLD signal in the ventral anterior cingulate cortex and the dorsal medial prefrontal cortex	15	No control	Short: reduction of nicotine craving	
	Gevensleben et al., 2009 [72]	EEG	Theta/beta ratio	102	Randomized controlled trial, neurofeedback vs attention Cognitive training	Short: improvement in the German ADHD rating scale	
ADHD	Lévesque et al., 2006 (Lévesque et al., 2006)	EEG	Slow cortical potential First phase:	20	Neurofeedback versus no treatment group	Short: reduction of ADHD symptoms in the neurofeedback group	Activity in the anterior cingulate cortex increased during a stroop task in neurofeedback group
	Gani, 2009 [73]	EEG	Neurofeedback on SMR and theta activity Second phase: Neurofeedback on theta and beta Slow cortical potential	47	Comparison with theta/beta ratio	Short: behavioural improvement (subjective) and decrease of ADHD scores  Long: effects persisted from 6 months up to 2 years after treatment	
	Steiner et al., 2014 [74]	EEG	Theta and beta	104	Randomized controlled trial	Short: symptom relief  Long: 6 month after training, effects remain	
Autism	Lam et al., 2020 [75]	fMRI	BOLD on right inferior frontal cortex	31	Randomised controlled trial	Short: clinical outcomes	
	Kouijzer et al., 2009 [76]	EEG	Theta, beta and SMR	14	Yes	Short: improvement of executive functioning	
	Kouijzer et al., 2010 [77] Thompson et al., 2010 [78]	EEG EEG	Theta power Beta and sensory motor rhythm	20 159	Yes No	Short: clinical outcomes Short: relief of symptoms, behavioural improvements	

Table 1 (Continued)

	Reference	NF Signal	Type of NF	Group size	Control	Short/long term effects	Behavioural and brain induced changes
Chronic pain, Tinnitus	deCharms et al., 2005 [79]	fMRI	BOLD on rostral anterior cingulate cortex	36	No but ability to control rACC activity predicts the effects on symptoms	Short: pain relief	
Mental retardation	Haller et al., 2013 [40]	fMRI	BOLD on auditory regions	6		Short: improvement of symptoms	
	Surmeli et al., 2012 [70]	EEG	Feedback on patient qEEG abnormalities	8	No	Short: behavioural improvement	
	Surmeli and Ertem, 2010 [80]	EEG	Feedback on patient qEEG abnormalities	23	No	Short: behavioural	
Learning disabilities	Fernández et al., 2007 (Fernández et al., 2007)	EEG	Theta alpha ratio	16	Placebo	Long: 2 years follow up, effects remain Short: behavioural	
	Becerra et al., 2006 [81]	EEG	Theta alpha ratio	10	Placebo	Long: no effect remaining after 2 months Long: 2 years after, spurt of EEG maturation, positive behavioural changes	
Healthy participant	Cho et al., 2004 [82]	EEG	Beta wave ratio	28	Control	Short: decrease of impulsiveness	
	Breteler et al., 2010 [83]	EEG	qEEG	19	Control group	Short: improvement in spelling	
	Lee et al., 2011 [84]	fMRI	Bold fMRI in insula	6			Changes in spatial activation pattern
	Ghaziri et al., 2013 [34]	EEG	Increase power of beta	30	Yes, sham or control group	Short: higher scores on visual and auditory attention	Changes in white and grey matter
	deBettencourt et al., 2015 [11]	fMRI	Decnef	16 per group	Sham feedback	Short: attention improvement	
	Cortese et al., 2016 [28]	fMRI	Decnef	18	No but comparison between two opposite feedbacks	Short: change in confidence	
	Amano et al., 2016 [29]	fMRI	Decnef	18	No but feedback on two different colours	Short: change in colour perception	

#### 4. Neurophysiological effects of neurofeedback

Neurofeedback-based cognitive training leads to clinical improvement in patients and enhanced behavioural performance in healthy participants. These effects can last up to 12 months and rely on the brain's ability to learn across its lifetime, in other words, on brain plasticity. In fact, numerous studies report neurophysiological changes triggered by neurofeedback training. These changes mainly correspond to general non-specific functional and structural changes in the learning networks, or functionally specific changes associated with the neuromarkers used during the neurofeedback procedure. For example, studies combining EEG-based neu-

rofeedback with fMRI imaging show that neurofeedback success is correlated with an increased activity in the thalamus suggesting that neurofeedback triggers reinforcement learning and brain plasticity [20,31]. A meta-analysis further shows that almost all neurofeedback protocols trigger an increased activation in the striatum, which also plays a crucial role in reinforcement learning [32]. In other words, neurofeedback behavioural effects rely on the success of the participants in learning to control their brain activity based on the success indicator they are given (ball position, gauge filling up, task difficulty changing etc.). In agreement with these results, a very recent study shows that neurofeedback success can be predicted by the volume of the putamen of the participants [33], indicating that prior participants learning abilities (as indexed by putamen volume) is predictive of how



well they will integrate and benefit from neurofeedback. Thus, neurofeedback effects rely on a combination of initial conditions, and neurofeedback induced structural and functional changes following cognitive training.

Neurofeedback induced plasticity is not restricted to structural or functional changes in the learning network, and can also be observed (expectedly) on the neuro-biomarkers used to drive the neurofeedback. For example, ADHD patients show increased white matter myelination and grey matter volume after neurofeedback in the functional networks involved in sustained attention [34]. Quite surprisingly, these changes are very rapid as they can be triggered after only a single one-long hour neurofeedback session [35,36]. Several studies additionally report changes in brain functional connectivity following fMRI neurofeedback. These changes are specific to the functional network targeted by the neurofeedback [37,38], including in neurofeedback protocols that are not directly driven by functional connectivity [35,39–41]. Indeed, changes in functional connectivity can be observed after an fMRI neurofeedback driven by BOLD fMRI signal from the right inferior frontal cortex of ADHD patients. These changes correspond to a decrease of the functional connectivity of the frontal cortex within the default mode network (DMN) and an increase in functional connectivity within the dorsal caudate and inferior cingulate (salience network) [39]. Most importantly, these changes correlate with behavioural improvement. Likewise, after an EEG-based neurofeedback driven by alpha oscillatory power, an increase of functional connectivity within the salience network and a decrease of functional connectivity within the default mode network can be observed, both correlating with the participants' success in the neurofeedback task [42]. Profound cortical reorganizations are also observed in clinical contexts, for example, following EEG-based neurofeedback in ADHD patients driven by the beta/theta EEG oscillatory power ratio. Specifically, a decrease in the power of theta frequencies is observed in the left frontal and cingulate regions, while an increase in alpha power is observed in the right temporal lobe and the right frontal regions, and an increase in beta power is observed in the left temporal, right frontal and cingulate cortex regions [43]. Likewise, in post-traumatic stress disorder patients, a change in the long-range temporal correlations in both the amplitude envelope of broad band signal and in the theta and alpha band oscillations from all brain sites can be observed after they have performed an EEG-based neurofeedback driven by alpha power amplitude. These changes are correlated with improved symptoms, thus questioning the link between long range correlations and oscillatory alpha power [44]. Given that these effects of neurofeedback on brain structure and function can be observed even after short sessions of neurofeedback, it has been suggested that these effects rely on classical Hebbian plasticity mechanisms [45], the overall effect of which is to maximize trial reinforcement outcome. However, little is known about the precise underlying neuronal mechanisms. In particular, it is not clear whether neurofeedback, which is by definition an ecologically implausible life experience, exclusively recruits pre-existing neuronal and network loops, or whether it triggers novel computational cortical capabilities that cannot be triggered by ecological conditions.

## 5. Is neurofeedback a golden tool for training plasticity?

Overall, there is thus ample reproducible evidence that neurofeedback can trigger behavioural and cortical plasticity changes that result in improved cognitive functions in both impaired and healthy participants (non-exhaustive summary in Table 1). However, it would be misleading to think that the benefit of neurofeedback protocols has reached consensus. Several limits of this type of protocols deserve attention and experimental consideration. Most of these issues are not specific to neurofeedback, but are relevant to all cognitive training approaches. First, while some studies report long lasting behavioural benefits of neurofeedback training, it is still unclear whether this applies to all neurofeedback approaches. Thus a systematic evaluation of neurofeedback effects at a distance from the intervention should be planned, possibly providing a better understanding of the functional and structural predictors of enhanced neurofeedback training benefit retention in time. Second, the Graal of cognitive training protocols, and in particular of neurofeedback, is training generalization, such that the enhanced behavioural performance observed in the main training protocol also results in enhanced cognitive capabilities in everyday life situations. This transfer of behavioural effects outside of the lab context is rarely tested, thus raising the central question of the behavioural and clinical relevance of neurofeedback outside the research context. Third, it is crucial to highlight the fact that, on average, neurofeedback results in 70 to 85% of the participants, called responders, to self-regulate their own brain activity [2,46]. The remaining 25 to 30% do not benefit from such approaches. These participants are called non-responders. This is not a minor issue as it means that up to 1/3 of a population of trained patients or volunteers are at risk of being insensitive to the treatment. This weakens one of the major advantages of the neurofeedback training relative to other cognitive training methods, namely its adaptability to patients and volunteers [47,48]. Studies have been conducted to understand why a substantial proportion of participants does not respond to self-regulation or neurofeedback training. This would allow to only select a priori responding participants in neurofeedback protocols, as well as possibly circumvent neurofeedback resistance by adapted protocols specifically tailored to individual subjects. These studies, rather than identifying a unique predictor of non-responsiveness, have on the contrary identified multiple indicators, ranging from brain structure [49], trust and understanding of the technology of the neurofeedback protocol [50], putamen volume [33] or resting state brain activity [51]. While such studies need to be pursued, this suggests that a fine tuning of the neurofeedback procedures to the baseline characteristics of the participants might help decrease the proportion of non-responders.

Another important issue associated with neurofeedback studies is the functional specificity of the reported effects. How can a simple alpha wave feedback really improve or repair a very complex function? Why would a global non-specific modulation of alpha/theta oscillatory power ratio lead to specific functional effects? Multivariate fMRI-based neurofeedback have started to address this issue, by considering

that neuronal signals recorded at any given time do not exclusively reflect a unique functions but rather multiple functions as well as complex interactions between these functions [11,12,29]. This has overall resulted in a more precise targeting of cognitive functions. For example, Cortese et al. demonstrate a very precise bidirectional targeting of individual participants' confidence in the task [12], thus achieving a precise manipulation of the associated cognitive function. Advanced targeting of cognitive functions is also under development in animal models using invasive recording techniques. For example, the locus of the attentional spotlight can be tracked at a very high spatial (below the 1°) and temporal resolution (circa 50ms) while subjects are performing complex cognitive tasks, using advanced machine learning techniques [14–18]. Based on these sophisticated methods, Gaillard et al. have shown that attentional neuronal processes are submitted to rhythmic ultra-slow fluctuations in the range of 4 to 5 cycles per hour, alternating between epochs of high efficiency and epoch a low efficiency [52]. Independently, Amengual et al. show that access to spatial attention can be further enhanced by a proper multivariate modelling of attention-independent sources of noise in the recorded neuronal population [53,54]. Because these studies rely on real-time signal processing, they are expected to highly enhance neurofeedback procedures. In addition to shedding a new light on cognitive functions [55], these approaches are expected to be directly transferrable to human patients implanted with ECoG electrodes. Moreover, the underlying methodology has recently been generalized to non-invasive human fMRI recordings [13]. Overall, this thus opens the way to much finer grained and informationally rich cognitive training neurofeedback protocols.

Last, and probably most importantly, recent critical reviews of neurofeedback research outcomes highlight the fact that a lot of the studies lack proper experimental controls (see Table 1 for non-exhaustive literature review on this point). Thus some of the reported effects might be “mere” placebo effects. Schabus et al. conducted a double blind EEG study to evaluate neurofeedback effects on insomniac patients [56]. Surprisingly, they observed improvements both on treated and placebo patients. They thus concluded that the neurofeedback effects can, in some studies, be due to a placebo effect arising for example from trust in the treatment or empathy from experimenters. This study has resulted in a strong debate regarding the caveats of ideological stands and financial biases in neurofeedback research, emphasizing the need for double blind and placebo studies [56–60].

In conclusion, this review highlights the fact that in spite of its current methodological limitations, neurofeedback is an efficient cognitive training tool, that has recently greatly benefited from signal processing and technological advances, as well as from a better understanding of its associated neural bases. Pursuing on these lines of effort, and achieved a better informational targeting of cognitive functions is expected to further enhance the benefits of these approaches.

## Disclosure of interest

The authors declare that they have no competing interest.

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