Using recent BCI literature to deepen our understanding of clinical neurofeedback: A short review

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Abstract

In their recent paper, Alkoby et al. (2017) provide the readership with an extensive and very insightful review of the factors influencing NeuroFeedback (NF) performance. These factors are drawn from both the NF literature and the Brain-Computer Interface (BCI) literature. Our short review aims to complement Alkoby et al.'s review by reporting recent additions to the BCI literature. The object is to highlight this literature and discuss its potential relevance and usefulness to better understand the processes underlying NF and further improve the design of clinical trials assessing NF efficacy. Indeed, we are convinced that while NF and BCI are

fundamentally different in many ways, both the BCI and NF communities could reach compelling achievements by building upon one another.
By reviewing the recent BCI literature, we identified three types of factors that influence BCI performance: task-specific, cognitive/motivational and technology-acceptance related factors. Since BCIs and neurofeedback share a common goal (i.e., learning to modulate specific neurophysiological patterns), similar cognitive and neurophysiological processes are likely to be involved during the training process. Thus, the literature on BCI training may help (1) to deepen our understanding of neurofeedback training processes and (2) to understand the variables that influence the clinical efficacy of NF. This may help to properly assess and/or control the influence of these variables during randomised controlled trials.
Overall, our review suggests that in order to adapt NF features, BCI machine learning tools may be used to identify more individualized NF features, with patient-specific frequency bands and brain areas. Additionally, performance predictors from sensorimotor (SMR) BCI research, e.g., mu rhythm at rest or gamma power in attentional networks, may be used to select whether SMR-NF is a suitable protocol for a given patient. Regarding feedback adaptation, tactile feedback might improve SMR-NF, while computerised social and emotional feedback (e.g., using learning companions) might help to improve motivation. Both have been explored by the BCI community. Finally, BCI algorithms could help identify optimal mental strategies for each patient based on a small number of trials. Mindfulness meditation training procedures and automatic difficulty adaptation, as used successfully in BCI, may also contribute to improving the clinical efficacy of NF.

Keywords

Neurofeedback; neurofeedback efficacy; brain–computer interfaces; training; EEG; adaptation; cognitive profile; personality

Introduction

Through their recent paper, Alkoby et al. (2017) provide the readership with an extensive and very insightful review of the factors influencing NeuroFeedback (NF) performance. These factors are drawn from both the NF literature and the Brain-Computer Interface (BCI) literature. Our short review aims to complement the review of Alkoby et al. by depicting some additional recent BCI literature. The object is to highlight this literature and discuss its potential relevance and usefulness to better understand the processes underlying NF and further improve the design of clinical trials assessing NF efficacy. Indeed, we are convinced that while they have fundamental differences, by building upon one another both the BCI and NF communities could reach compelling achievements.

As extensively described in Alkoby et al. (2017), the efficacy of clinical NeuroFeedback (NF) is subject to significant between-patient and between-study variability. The clinical efficacy of NF is heavily debated, particularly regarding psychiatric disorders. For this reason, this paper is devoted specifically to clinical NF. Some researchers indeed suggest that the clinical efficacy of NF is underlain by a placebo effect (Thibault et al. 2017). We agree that the level of evidence is still weak concerning the clinical efficacy of NF, and that a placebo effect may be involved to some extent. However, it is unlikely that this lack of evidence is due to the fact that NF is fully underlain by a placebo effect. Rather, we hypothesise that it may be due to the lack of Randomised Controlled Trials (RCT) assessing NF learning effects. Yet, in order to rigorously estimate these learning effects, and provide a higher level of evidence for the clinical efficacy of NF, the variables influencing these effects should first be identified. In this paper, we argue that recent BCI results could be relevant and useful to identify such variables and help us deepen our understanding of the clinical efficacy of NF.

As stated by Sitaram et al. (2016) "*much remains to be investigated, including the integration of the vast knowledge of training and learning psychology into NF protocols*". Thus, a human-factor-centred standpoint, considering the influence of the technology and the way it was designed on patients' achievements (Sanders & McCormick, 1993) is required. A human-factor-centred standpoint would take into account the interaction between the patient and the system during the NF procedure. Such an approach could help us understand how various factors affect the ability of patients to learn to modulate the target neurophysiological pattern – *i.e.*, the EEG feature(s) that the patient is learning to self-regulate (*e.g.,* alpha rhythm power, the theta/beta power ratio, etc.) – during NF training (Micoulaud-Franchi, McGonigal et al. 2015; Arns, Batail et al., 2017). These include factors such as the design of the NF training protocol (*e.g.,* type of feedback), the neurophysiological features, and the states (*e.g.,* motivation) and traits (*e.g.,* self-reliance) of the users (Jeunet et al., 2015b). This human-factor-centred standpoint was adopted in the review by Alkoby et al. (2017), in which the authors depict many factors that affect NF efficacy. Their goal in doing so was to promote the use of these factors to adapt NF training protocols to the user's personality, and to their cognitive and neurophysiological profiles. In order to adapt these training protocols, the authors propose to focus on three aspects: neurophysiological features, feedback and mental strategies.

Although their review is already extensive and very instructive, further insight can be gained by studying the recent literature on training and learning in the field of Brain-Computer Interfaces (BCIs), and more specifically in the field of Mental-Imagery based BCIs (MI-BCIs) (Wolpaw & Wolpaw, 2012; Jeunet et al., 2016). MI-BCIs differ from NF in that the goal of MI-BCIs is to control an application without moving, by modulating specific brain rhythms through the completion of Mental-Imagery (MI) tasks. These tasks can be motor-imagery tasks, such as imagining moving one's hands (Pfurtscheller & Neuper, 2001), or non-motor-imagery tasks, such as mental calculation or mental rotation (Friedrich et al., 2012, Jeunet et al., 2015b), all these mental tasks being detectable in EEG signals. The rationale for this approach is that performing each of these mental-imagery tasks will induce modulations of different brain rhythms, which are theoretically specific to each task. Each task is associated to a specific control command, such as "imagine left-hand movements to turn the wheelchair towards the left" and "imagine right-hand movements to turn the wheelchair towards the right" (Clerc et al., 2016). Thus, the system is able to detect modulations of the user's brain activity and determine which command the BCI user intended to send. For instance, a decrease in mu amplitude over the left sensorimotor cortex should occur when users imagine a right-hand movement, i.e., when they want to turn right (Pfurtscheller & Neuper, 2001).

Both NF and MI-BCI users need to learn to regulate their neurophysiological EEG activity, using the feedback they are provided with, in order to produce specific EEG patterns (Sherlin et al., 2011; Strehl, 2014; Neuper & Pfurtscheller 2009; Lotte et al., 2013). The objective is either to reach a target EEG pattern in NF (Sherlin et al., 2011; Strehl 2014; Gruzelier, 2014a) or to produce a given EEG pattern that can be translated into a given command for an application in BCI (Neuper & Pfurtscheller 2009; Lotte et al., 2013; Clerc et al., 2016). Consequently, similar cognitive and neurophysiological processes are likely to be triggered during both BCI and NF training procedures. Thus, we advocate considering the literature on BCI training to deepen our understanding of NF efficacy – in the same way that the BCI community should avail themselves of the NF literature.

First, we attempt to give a brief review of the relevant BCI literature, in order to complement the review by Alkoby et al. (2017). Indeed, the BCI community is also currently investigating the factors that influence user performance, training and learning. Notably, three main categories of factors were identified based on a review of the literature (Jeunet et al., 2016):

task-specific factors, cognitive and motivational factors and technology-acceptance[1] related factors. We suggest that these factors could be relevant for clinical NF training as well. Next, we elaborate on the potential implications of this research for improving the design of NF sessions and clinical NF efficacy, *i.e.*, to reduce the clinical symptoms to which the target neurophysiological patterns are associated. We conclude with a summary and a diagram that outlines a framework, which takes into account the different factors identified in the review, in order to deepen our understanding of EEG signal self-regulation during NF, thereby potentially improving the clinical efficacy of NF[2].

Adapting the neurofeedback training protocol using a human-factor-centred standpoint

In the coming section, we provide information from the BCI training literature that could be relevant to adapt NF procedures to each patient, following the structure used by Alkoby et al. (2017), namely: (1) adapted neurophysiological features, (2) adapted feedback and (3) adapted mental strategy. Each of these three sections covers the factors belonging to each of the three categories mentioned in the introduction: task-specific factors, cognitive/motivational factors and technology-acceptance related factors. As the name suggests, *task-specific* factors are those that are directly concerned with helping each individual user to self-regulate target neurophysiological patterns. *Task-unspecific* factors, on the other hand, are those that may indirectly affect the patients' ability to regulate target neurophysiological patterns. These task-unspecific factors include "cognitive/motivational" and "technology-acceptance related" factors, which can be altered with the aim of indirectly improving performance and NF efficacy, by modulating patients' psychological states for instance.

Adapting the neurophysiological features

While in most NF research studies, only one or two channels and a fixed frequency band are used (Gruzelier 2014a; Micoulaud-Franchi et al., 2014), most MI-BCI systems use a combination of multiple channels and a frequency band adapted to each user (Nam et al., 2018). This is usually achieved using Machine Learning (ML) tools that can identify EEG features with the highest signal-to-noise ratio (SNR) for each user, based on examples of this user's EEG signals (Blankertz et al., 2006; Vidaurre et al., 2012; Höhne et al., 2014).

[1] The name of this category of factors was inspired by the "technology-acceptance model" (Venkatesh and Davis, 2000). This model depicts the factors that affect the use and acceptance of technologies by their users

[2] As stated earlier, this short review is intended to complement Alkoby et al.'s (2017) review in the same special issue. Thus, we advise reading both papers together.

For instance, ML tools are extensively used to identify user-specific SensoriMotor Rhythm (SMR) frequency bands in SMR-BCI[3] (Pregenzer et al., 1999; Blankertz et al., 2008, Ang et al., 2012). In the future, such tools might lead to improved individualized NF features, with a higher SNR, going beyond heuristics like Individualized Alpha Frequency (IAF) (Bazanova et al., 2010). Moreover, ML algorithms are also used to automatically identify functionally-specific cortical sources, e.g., SMR sources (Blankertz et al., 2008, Vidaurre et al., 2012) or attention-related sources (Hamadicharef et al., 2009). Such sources are defined as the individual EEG channels (Lal et al., 2004; Arvaneh et al., 2011) or combination of channels, i.e., spatial filters (Blankertz et al., 2008; Lotte & Guan, 2011; Samek et al., 2014), which record the greatest modulation of EEG activity during a given task. ML tools have proven key to improving the SNR of EEG features in MI-BCI. This allows MI tasks to be recognised more accurately than when using fixed channels and fixed frequency bands (Müller et al., 2008, Höhne et al., 2014). Learning to self-regulate SMR was also improved (Vidaurre et al., 2012), including in MI-BCIs relying on a NF-based training procedure (McFarland et al., 2011). Thus, such methods seem to be worth exploring for EEG-NF. They may also improve the SNR of EEG-NF features and the efficacy of self-regulation learning. Interestingly, ML tools have also been successfully used in fMRI-NF, with so-called "decoded NF" approaches (Shibata et al., 2011, Cortese et al., 2016, Sitaram et al., 2016). This further emphasizes their potential for EEG-NF.

The works mentioned hereinabove focus on directly helping patients to regulate the target neurophysiological feature. As mentioned before, some task-unspecific factors - which can be quantified in EEG features - have also been identified as predictors of BCI efficacy and thus may potentially predict NF efficacy as well. Notably, both mu rhythm amplitude at rest, and gamma power in attentional networks during BCI control have been shown to correlate with SMR-BCI performances (Blankertz et al., 2010, Grosse-Wentrup et al., 2011). More specifically, SMR-BCI control performances correlate positively to mu rhythm amplitude at rest in the C3 & C4 channels (Blankertz et al., 2010), and to gamma power in frontal and occipital brain areas (Grosse-Wentrup et al., 2011), whereas they negatively correlate to gamma power in centro-parietal areas (Grosse-Wentrup et al., 2011). Thus, these two task-unspecific cognitive/motivational predictors may be used, possibly alongside other predictors (Alkoby et al., 2017), to predict whether a given patient is likely to be able to self-regulate

[3] SMR-BCI are BCI that translate variations of SMR activity into control commands (Yuan & He, 2014). Such variations can be achieved using motor imagery or any other self-regulation as used in SMR-NF.

his/her SMR with SMR-NF, or whether another NF protocol might be more promising, e.g., Slow Cortical Potential or Theta/Beta Ratio for ADHD treatment.

A relevant technology acceptance-related factor that has also been identified is the sense of agency (SoA) (Vlek et al., 2014), which can be defined as the feeling of control that the user experiences when interacting with a technology (Kilteni et al., 2012). In the case of NF, the sense of agency could be defined as the extent to which patients feel they have control over the feedback they are provided with. The sense of agency has been shown to positively correlate to both BCI and NF performances: several studies have revealed a positive correlation between SMR-BCI performance and the results of various questionnaires designed to measure the feeling of control (reviewed in Jeunet et al., 2016). Furthermore, a recent study revealed that manipulating a robotic hand feedback to increase the SoA (measured using a questionnaire) leads to stronger SMR modulation in a NF training procedure (Braun et al., 2016). The neural correlate of the sense of agency involves activity in the Pre-Motor Cortex (PMC) (David et al., 2008). Thus, the SoA, measured either with questionnaires (offline) or with its neural correlate (PMC activity, potentially measurable online), could be used as a task-unspecific feature to predict whether a given NF protocol is likely to favor self-regulation. It could also be used to adapt the feedback in order to increase the SoA and thus possibly self-regulation (see also next section).

Overall, these BCI results may provide useful tools for NF training, in particular:

- Available BCI machine learning tools may help to design more individualized task-specific NF features, with patient-specific frequency bands and brain areas.
- Some task-unspecific features identified in BCI research may prove useful for NF training as well. They include the mu rhythm at rest, gamma power in attentional networks and PMC activity reflecting the SoA. Such features might be used alongside other predictors to select whether SMR-NF is the best protocol for a given patient, or whether other protocols (e.g., SCP or Theta/Beta ratio for ADHD rehabilitation) would seem more likely to succeed.

Adapting the feedback

When designing the feedback, both its form/style and its content/substance must be considered. Indeed, both may potentially influence the clinical efficacy of NF.

Concerning the form of the *feedback*, beyond visual feedback, broadly depicted in the review of Alkoby et al. (2017), other sensory modalities may be relevant. First, auditory feedback has been used for BCI training (Hinterberger et al., 2004; Gargiulo et al., 2012; McCraedie et al., 2014) and has been experimentally proved to be as effective as visual feedback despite being slower (Nijboer et al., 2008). Second, tactile feedback has also been tested and shown to be comparable to visual feedback for motor-imagery based BCIs (Kauhanen et al., 2006; Cincotti et al., 2007; Chatterjee et al., 2007; Leeb et al., 2013). In some cases, it has even been shown to be better: when proprioceptive feedback was provided using a robotic arm (Gomez-Rodriguez et al., 2011) or when vibrations were provided on the hands, during hand motor-imagery, using vibrotactile motors (Jeunet et al., 2015). Besides, providing tactile feedback could improve the sense of agency, i.e., a *technology acceptance-related factor*, in motor-imagery based BCIs (Thurlings et al., 2012). In turn, experiencing a high sense of agency could increase the feeling of mastery and consequently reduce perceived difficulty, increase motivation, and potentially improve performance (Vlek et al., 2014). Based on these results, we may hypothesise that tactile feedback could also be relevant for SMR-NF. An interesting research question in the future would be to investigate whether some sensory modalities might be more relevant/efficient for providing feedback depending on the NF paradigm, i.e., depending on the EEG frequency band targeted.

Furthermore, regarding the content of the feedback, some types of feedback can greatly influence performance no matter which task is being performed (i.e., whatever the target neurophysiological patterns). We call this type of feedback "task-unspecific feedback". For instance, while cognitive feedback (i.e., feedback providing information about the task) is extensively investigated in NF research protocols, emotional and social feedback is often neglected. Yet, social interaction is of utmost importance during the learning process (Kort et al., 2001), including the NF learning process (Sherlin et al., 2011; Gevensleben et al., 2012). Therefore, emotional support and social presence should also be provided in NF controlled research protocols (just as they are provided by therapists during NF therapy). Their influence on the outcome of the NF training procedure should be assessed. In this view, emotional feedback has been studied (Kübler et al., 2001) and the positive impact of multiplayer/social feedback demonstrated (Bonnet et al., 2013; Nijholt, 2015). Also, Pillette et al. (2017) showed that providing emotional support and social presence using a learning companion improved user-experience during the MI-BCI training procedure. In the same vein, studies (Barbero and Grosse-Wentrup, 2010; Kübler et al., 2001b) report that when provided with positively biased feedback, novice MI-BCI users' performance increases. However, this effect does not persist once they have progressed to the level of expert users. This could be because positive feedback provides users with an illusion of control, which increases their motivation and their will to succeed. As explained by Achim and Al Kassim (2015) once users reach a higher level of performance, they also experience a high level of self-efficacy which leads them to consider failure no longer as a threat (Kleih et al., 2013) but as a challenge. Facing these challenges leads to improvement. The effect of cognitive/emotional factors (such as emotional and social support) on the efficacy of NF training procedures in terms of performance and user experience may be worth investigating in NF research.

To summarize, the following elements may be worth being tested in NF training procedures:

- Adapting the feedback, and especially its associated sensory modality, to the target neurophysiological patterns when relevant (e.g., tactile feedback for SMR-NF).
- Favouring motivation, *e.g.*, by providing emotional support and social presence adapted to patients' states and traits.
- Improving technology-acceptance, *e.g.*, by providing a positively biased feedback to novices so that they experience a higher sense of agency.

Adapting the mental strategy

Both BCI and NF results suggest that the mental strategy that patients use could and should be adapted (Strehl 2014; Fruitet et al., 2013). In the BCI literature, Neuper et al. (2005) suggested that prompting users to perform kinaesthetic rather than visual motor imagery improves SMR-BCI performances. Results from (Fruitet et al. 2013) suggested that identifying subject-specific mental strategies to modulate SMR activity in an MI-BCI increased performances. They also proposed a Bandit algorithm to efficiently identify the most promising strategies with as few trials as possible (Fruitet et al., 2013). In the NF literature, as reviewed in Strehl (2014), it is recommended not to impose nor suggest a single specific strategy to subjects, but rather to let them identify the strategy that suits them best by themselves. Additionally, Kober et al. (2013) also suggest that users who do not use any deliberate mental strategy (N=4 in their study) may obtain better SMR-NF performances than those who do (e.g., imagining movements or focusing on the feedback gauge). Taken together, these results suggest that different mental strategies, including possibly no strategy, could lead to stronger self-modulation of brain rhythms in NF. Bandit algorithms developed for BCI (Fruitet et al., 2013) may prove useful for NF, and may help to identify the best mental strategy to modulate a given brain rhythm (which could be “no strategy”), with a minimal number of trials. There are also task-unspecific strategies that may be employed to further improve NF efficacy. Notably, automatic difficulty adaptation of the BCI/NF training seems promising at the cognitive and motivational levels (Lotte et al., 2013; Strehl 2014). This can indeed be a form of shaping, i.e., operant conditioning reinforcing successive approximations of the target skill (Strehl 2014). In NF, automatic threshold adaptation is often used, with a fixed reward rate, e.g., 60% or 70% (Sherlin et al., 2011; Strehl 2014). However, this method has been criticized as it does not ensure the reinforcement of overall progress and may even reinforce progress in the wrong direction (Sherlin et al., 2011; Strehl 2014, Arns et al., 2014), thus highlighting the need for new methods (Strehl 2014). Recent BCI studies have proposed to adapt task difficulty to favour the state of Flow (Csikszentmihalyi & LeFevre, 1989), a state of optimal experience favouring learning and performance in general (i.e., not only in BCI/NF). In Mladenovic et al., (2017), adapting the feedback bias in each trial, according to the user’s performances, led to an increased Flow state (measured using a questionnaire). Since favouring the Flow state is thought to improve learning (Csikszentmihalyi & LeFevre, 1989), and since a recent model of NF proposed a theoretical relationship between the Flow state and NF performance (Gaume et al., 2016), this suggests such BCI methods might also benefit NF training. Interestingly, recent NF-based BCI training works also suggest that difficulty thresholds could be automatically adapted according to the users subjective mental efforts (Bauer et al., 2016) or progressively with constraints ensuring that learning goes in the desired direction (Dindhsa et al., 2017), both of which may lead to improved BCI/NF performances. Finally, concerning technology-acceptance, computer anxiety has been shown to impair BCI performance (Jeunet et al., 2015b). Computer anxiety is a state anxiety (Chua et al., 1999) perceived when interacting with a computer. This term was first proposed some 30 years ago when people were not yet familiar with computers. Today, one could argue for extending this term to describe the apprehension users perceive when confronted to new technologies. Technologies may have both a positive or negative influence on patients’ responsiveness to NF. Indeed, as stated by Thibault et al. (2017), “neurofeedback demands high engagement and immerses patients in a seemingly cutting-edge technological environment over many recurring sessions, [which] may represent a powerful form of placebo intervention”. Those authors state that NF efficacy could be increased due to a placebo effect related to the technology. If such a placebo effect exists for some patients, a nocebo effect (due to the computer anxiety phenomenon) may occur for others. Therefore, adapting BCI/NF training in order to reduce users’ anxiety may improve BCI/NF performances. For instance, NF users could be trained to meditate before they start NF training (Evans et al., 2008). Indeed, mindfulness meditation has already been shown to improve SMR-BCI performances (Tan et al., 2014). Meditation is also known to improve attentional abilities (Brandmeyer & Delorme 2013), which are positively correlated to BCI performances (Jeunet et al., 2016). As such, training users to mindfulness meditation before NF training might be a task-unspecific way of improving their subsequent performances.

To summarize, the works reviewed above suggest that:

- Further research is needed to identify the best mental strategies, and to determine whether a specific and deliberate strategy is useful (Strehl 2014). Bandit algorithms used in BCI could help to identify such strategies for each patient, based on a small number of trials (Fruitet et al., 2013)
- Task-unspecific strategies that proved useful in BCI, such as automatic difficulty adaptation (Mladenovic et al., 2017; Bauer et al., 2016, Dindhsa 2017) or training users to mindfulness meditation (Tan et al., 2014), ought perhaps to be considered for NF as well.

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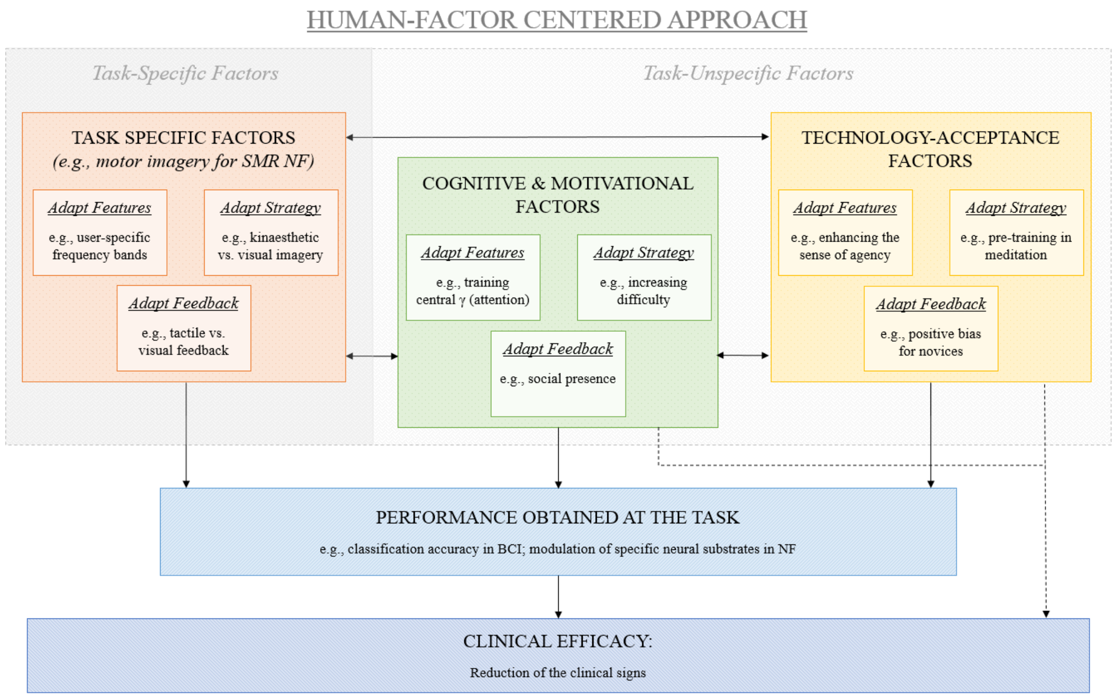

Figure 1: This figure summarises the human-factor-centred standpoint which stems from the literature on BCI training. His standpoint could be of interest to the field of neurofeedback in order to deepen our understanding of EEG signal self-regulation and thus potentially improve NF clinical effectiveness. We divided the factors that have been suggested to influence performance and clinical effectiveness into 3 categories. The first category (left) contains task-specific factors while the second and third categories, "motivational and attentional variables" and "technology-acceptance variables" contain what we propose to call "task-unspecific factors". Concretely, the NF procedure targets a specific target neurophysiological pattern, the modulation of which can be influenced by the adaptation of specific neurophysiological features/feedback/mental strategies. Research has shown that to learn to self-regulate the target neurophysiological pattern (and thus potentially influence the clinical effectiveness of the procedure), certain task-unspecific factors ought perhaps to be considered.

Task-specific and task-unspecific variables influencing the efficacy of clinical neurofeedback

The literature reviewed in the previous sections suggests that adapting training protocols to each user based on human-factors may help to improve BCI learning efficacy. It seems relevant to reinforce this practice in RCT evaluating clinical NF procedures, with the goal of optimizing the level of evidence concerning clinical NF efficacy in patients with mental/brain disorders.

As emphasized by Arns et al. (2014) many double-blind Randomised Controlled Trials (RCT) are very well designed regarding the clinical trial itself, but strangely enough the design of the NF training sessions is often barely described. Moreover, the ability to learn to modulate specific neurophysiological patterns is very rarely analyzed and reported in RCTs aiming to demonstrate the efficacy of NF (Zuberer et al. 2015; Sherlin et al. 2011). Nevertheless assessing the learning process in NF studies is fundamental (Arns, Heinrich et al. 2014; Gaume, Vialatte et al. 2016; Gruzelier, 2014b). As Rémond & Rémond stressed: "*Doubting the efficacy of a biofeedback treatment on a physiological variable when this treatment is carried out without previously testing the modification of this variable, is the equivalent of doubting the efficacy of a drug to cure a disease when the drug has not been absorbed by the patient*" (Rémond and Rémond 1997, Micoulaud Franchi and Fovet 2016). In other words, the remaining challenge for assessing the efficacy of NF therapies is to develop rigorous standards that ensure the consistency (*i.e.*, fidelity - Gevensleben et al., 2012, Micoulaud-Franchi, Salvo et al. 2016) of NF training protocols, in order to optimize the potential positive effects of NF. However, while very relevant guidelines have been outlined (Enriquez-Geppert et al., 2017; Gruzelier et al., 2014b, Sitaram et al., 2016), no "optimal" NF training procedure has been defined as yet. Nevertheless, many NF practitioners claim that, in addition to rigorous technological aspects of NF, a human factor-centered approach is central in the efficacy of NF therapies (Sherlin et al., 2011; Vollebregt et al., 2014; Zuberer et al., 2015; Strehl 2014; Mayer et al. 2015). In particular, Strehl (2014) stressed that "*the therapist will need to know the laws of learning as well as how to apply neurofeedback training in order to be a competent partner*". The limitation of such a position is that currently these skills rely on clinical experience (Gevensleben et al., 2012) rather than on scientific knowledge related to NF learning processes (Sherlin et al., 2011; Vollebregt et al., 2014; Zuberer et al., 2015). Thus in order to improve the consistency, quality and efficacy of NF sessions, several requirements should be considered, as proposed recently in (Arns et al., 2017, Sitaram et al., 2017):

- The identification of a framework of factors to be controlled for (Arns et al., 2017, Enriquez-Geppert et al. 2017).
- The assessment of each of these factors based on scientific evidence (Sitaram et al. 2016).

Among these factors, we stress in this article that human-factor centred criteria should be considered as central and should not be considered scientifically non-measurable. As shown in the Section "*Adapting the neurofeedback training protocol using a human factor centered standpoint*", the evidence brought to light in recent work in the field of BCI training could be of interest in the field of NF for two reasons. First, to better control factors that influence the NF training process in future double blind RCTs, and second, to improve clinical NF efficacy.

Interestingly, the framework proposed in Figure 1 for clinical NF might enable us to gain a better understanding of the respective contributions of the placebo effect and the specific clinical effectiveness of learning to self-regulate target neurophysiological patterns (Hammond, 2011), as well as the interaction between both. Indeed, the "cognitive/motivational" and "technology-acceptance related" factors, which were discussed in the section entitled "Adapting the neurofeedback training protocol using a human factor centered standpoint", could also contribute to the placebo effect, thereby influencing the clinical efficacy of NF. For instance, several factors have been suggested to have a positive effect on clinical symptoms by influencing the neurophysiological systems underlying the symptoms, but without necessarily influencing the neurophysiological patterns targeted in NF treatments (Hammond, 2011, Gaume et al. 2016). These factors are consistent with factors highlighted in the literature for influencing BCI performance: activating the attentional networks (Blankertz et al., 2010, Grosse-Wentrup et al., 2011), experiencing a flow state (Mladenovic et al., 2017, Bauer et al., 2016), a high sense of agency (Vlek et al., 2014; Jeunet et al., 2016; Braun et al., 2016) and being provided with positive social support (Pillette et al. 2017). The present framework suggests that we should not disregard these factors since they may contribute to the placebo effect (Thibault et al. 2017, Raz et Michels, 2007). Indeed, while RCTs should be performed in a manner that enables to control the placebo effect, the interpretation of this effect should not be oversimplified. For instance, Thibault and Raz (2016) emphasize the role of psychosocial variables to explain the efficacy of NF without fully considering how these factors could be integrated in a theoretical framework for NF. Thibault and Raz seem to simplify the issue by suggesting that the impact of NF is solely based on a technology-driven placebo effect. If this is the case, then the effects of NF are based entirely on the patients' perceptions of their own thoughts/feelings (and underlying brain activities) and the social reinforcement linked with the environment of an NF session. Yet the effect of NF could be based on two different mechanisms, that may be qualified as "task-specific" and "task-unspecific". On the one hand, the effects of NF could be due specifically to the self-regulation of target neurophysiological patterns, performed in order to reduce the clinical symptoms related to a given disorder. This is what we call a "task-specific mechanism", which is the mechanism that one would expect when performing NF training procedures. On the other hand, the effects of NF could also be based on the successful, but task-unspecific, regulation of brain activity (i.e., retrieving brain flexibility) (Ros et al. 2014). In other words, these effects could be related to some form of cognitive training which might occur during NF procedures, and which is nonspecific to the neurophysiological pattern targeted by the NF procedure. We call this mechanism a "task-unspecific mechanism". Interestingly, the framework we propose (see Figure 1) suggests that task-unspecific factors could also have a significant impact on the modulation of target neurophysiological patterns in NF treatments. Thus, beyond the debated placebo effect of NF (Thibault and Ras, 2016; Micoulaud-Franchi & Fovet, 2016), a human-factor-centred approach of NF leads us to consider the reciprocal influence of neural networks activated by the target neurophysiological patterns and those activated by the task-unspecific factors. As shown in the section "Adapting the neurofeedback training protocol using a human factor centered standpoint", the variables identified in the recent BCI literature could be very relevant to better understand the specific and nonspecific factors related to NF clinical efficacy.

Conclusion

As highlighted in this paper, more and more effort is devoted to the understanding of between-patient variability and to the control of between-study variability. In this view, Enriquez-Geppert et al. (2017) have provided a set of machine-related guidelines to design rigorous NF protocols and control between-study variability. In addition, Gaume et al. (2016) and Sitaram et al. (2016) have proposed a theoretical description of the neuropsychological and neurophysiological factors underlying NF training and learning, that could at least partly explain between-patient variability. The paper by Alkoby et al. (2017) and this paper offer complementary reviews of the literature regarding the factors which have been experimentally shown to correlate with NF/BCI performance.

Thus, Gaume et al. (2016) and Sitaram et al. (2016) use a top-down approach (they reflect upon theories in order to explain experimentally observed variability) while Alkoby et al. (2017) and ourselves chose to adopt a bottom-up approach (using experimental results as a starting point and suggesting explanations in the light of existing theories). Despite the different approaches, many conclusions are similar. In particular, it is clear that the neurophysiological features, the feedback and the mental strategies can and should be adapted to each patient to optimize clinical NF efficacy.

Nevertheless, the different papers reviewed suggest that in order to better understand the processes underlying clinical NF efficacy (and potentially improve this efficacy), we should not focus solely on the neurophysiological features, feedback and strategies directly related to the target neurophysiological patterns. Instead, both theoretical (Gaume et al., 2016) and experimental (Jeunet et al., 2016) reviews demonstrate the necessity to also consider task-unspecific factors, here depicted as "Cognitive and Motivational factors" and "Technology-Acceptance factors". Indeed, both the top-down/theoretical and bottom-up/experimental approaches report these factors as being involved in NF/BCI efficacy. For instance, Gaume et al. (2016) claim that self-agency, self-mastery, self-fluency and autonomy should be promoted. I the present paper, these factors are included in the technology-acceptance category (and in the user-technology relationship category in Jeunet et al., 2016). Moreover, Gaume et al. (2016) stress the importance of motivation, attention and working memory abilities. These factors are included in the Cognitive & Motivational factors category (or attentional and motivational factors category in Jeunet et al., 2016). This consistency between theoretical and experimental results is extremely promising for the future for two main reasons. First, it suggests that several relevant factors ought perhaps to be considered in order to improve of the clinical efficacy of NF. Second, as we are able to measure some of these factors (using questionnaires or neurophysiological measures) training procedures could be adapted accordingly (Mladenovic et al., 2018).

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