

The neural representation of self and neurofeedback and its application to the evaluation efficacy for smoking cessation

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Abstract: A recent synthesis of neuroimaging results identified two dorsal midline areas as candidates for the neural representation of self; one area is in the medial prefrontal cortex and the other in the precuneus. Each area is at the center of a cluster of areas identified in Theory of Mind tasks, which in turn, is surrounded by areas of the default mode network. A new framework is proposed for the way these areas fit the large network organization of the brain which leads to two important unifications. First the same neural networks are seen to handle attention and memory during awake state and sleep, but fulfilling different and complementary roles in each case. Second, the apparent diverse effects of neurofeedback are seen as consequences of stabilizing the midline neural representation of self. Finally, an operational way of applying the new framework is proposed and early results are presented in the context of evaluating neurofeedback interventions for smoking cessation.

Keywords—*neurofeedback, neurofeedback evaluation, neural representation of self (NRS), midline self-representation core (MSRC), default mode network, zone of proximal development (ZPD), comfort zone (CZ)*

I. INTRODUCTION

We are witnessing an unprecedented expansion of the methods available for non-invasive monitoring of the activity of the central nervous system. This proliferation of methods is accompanied by a dramatic increase in the details that can be extracted from the main neuroimaging methods of functional magnetic resonance imaging (fMRI) [1, 2] and magnetoencephalography (MEG) [3]. The older method of electroencephalography (EEG) is also getting a new lease of life. Better modeling of the head conductivity becomes a more realistic proposition thanks to the availability of enough computer power to do the task, even with modest computer hardware. Neurofeedback (NF) is an old intervention, which originally was entirely based on EEG. EEG NF for years was on the sideline of clinical practice because (a) Its approach was not easily incorporated within the established clinical practice, (b) EEG itself was not trusted to be relevant for reliable intervention, and (c) There was no framework providing candidate mechanisms through which NF may work. Since the start of the millenium medicine and neuroscience face all these concerns and either provide solutions or carve ways of properly addressing them: (a) The symptom based approach that dominated medicine is slowly but surely being replaced by a more organic view of medicine where the genetic and increasingly other defining properties of a person must be taken into account for health management. This movement is

spearheaded by the Research Domain Criteria (RDoC) initiative [4]. We are witnessing a new era of personalized medicine and in this brave world of medicine NF is not out of place, but firmly within the prevailing spirit of medical services. (b) The capability of a person to modulate his/her brain activity either at the level of EEG frequency or focal change in regional brain activity can now be demonstrated with MEG and fMRI; furthermore evidence accumulates that such changes influence health [5]. (c) A new framework for learning, attention and memory is introduced drawing on awake state studies [6] and MEG sleep studies [7, 8]. The analysis of sleep MEG data highlight the role of gamma band changes in activity patterns across the sleep stages in two well-defined brain areas that, for reasons that will become apparent later, are labelled the midline self-representation core (MSRC) [9]. Within this new framework NF can be understood as an attempt to push gently aberrant functioning of the MSRC towards the normal physiological patterns. Importantly, this normalization recruits, rather than opposes, natural mechanisms. These natural mechanisms appear to be erected by evolution to protect the integrity of the MSRC [9].

In the next section, a summary of a new framework for learning is outlined and the pivotal role of MSRC sketched (section II). The general framework describes interventions in general and NF intervention in particular as types of learning (section III). The next (section IV) discusses how the general framework can be used to provide personalized, quantitative measures of learning (efficacy of interventions) from single or double differentials of tomographic estimates of whole brain activity extracted from resting state EEG data. An example of measures of efficacy is provided in the next (section V) from a recent project on smoking cessation with NF. The paper ends with a short set of conclusions (section VI).

II. A GENERAL FRAMEWORK AND THE NEURAL REPRESENTATION OF SELF

A. Generalization of concepts from psychology

The new framework is founded on terms borrowed from psychology and cloaked with what one might call the standard model of modern neuroscience. The neural representation of self is described first, followed by the three basic concepts of developmental psychology: assimilation, accommodation, and zone of proximal development (ZPD). The full logic behind these redefinitions is fully described in [9]. Here, space limitation allows us only to state the results and sketched how

the new framework unites the way attention and memory facilitate learning during the day and night.

B. The midline self-representation core

Recently, neuroimaging studies have emphasized a collection of brain areas that consistently show more activity during resting state than active tasks, collectively termed the Default Mode network (DMN) [10,11]. The DMN is spread over large parts of the brain. Many authors have attempted to relate the DMN, or parts of it, to the concept of self [12, 13], especially its nodes closer to the midline. Other studies have also suggested independently that areas close to the midline might be related to the neural representation of self (NRS) [6, 14].

In our 2009 analysis of sleep MEG data, we searched for consistent changes in brain activity across sleep stages. After considerable effort we identified only a small number of areas whose gamma band activity during the quiet “core” periods of each sleep stage seemed to increase from the awake state, through light and deep sleep, culminating in the highest activity during REM sleep [7]. The two most prominent areas are in the dorsal part of the left hemisphere, making up what we have termed the midline self-representation core (MSRC), with MSRC1 and MSRC2 representing its rostral and caudal parts, see Fig. 1 of reference [9] for details.

When the areas defined by DMN, and self-related tasks are put together with the MSRC in a common template brain, a three layer double onion structure emerges with the MSRC network at its core: with MSRC1 at its anterior and MSRC2 at its posterior pole. The outermost layers are best activated with tasks of maintenance of the state when no imminent action is needed, i.e. the classic DMN resting state condition. The intermediate layer, closer to the core is activated in tasks accessing self-referential information, meta-cognition and autobiographical memories, usually referred as Theory of Mind (ToM) tasks [15]. The core itself shows best during REM sleep but it begins to show in tasks where fine separation between first and third person descriptions is needed [16, 17]. For the reasons mentioned above and the more complete explanation given in [9] the MSRC brings us a step closer to defining the neural representation of the core self. A detailed study of events leading to highly rhythmic spindle activity and the large amplitude K-complexes [8, 9] suggests that the MSRC is least active in awake state and emerges during spindle activity, a period when memory consolidation is believed to take place [18] and becomes even stronger during REM.

C. Assimilation, accommodation and ZPD

Assimilation is defined as brain activity for processing internal or environmental events, leading to resolution (not necessarily with conscious awareness and/or understanding) and action that require little to no significant change in the neural networks of an individual’s brain; the changes during assimilation can be regional taking place in sensory specific areas or multimodal areas far away from the MSRC.

Accommodation is defined as any process that requires some modification of the internal model of the world to “accommodate” new experiences that could not be (fully)

accounted for during the first encounter. Routine accommodation may involve some major change in the internal representation of the world but only little re-adjustment of the part that influences or contains our own self-image, i.e. MSRC.

An assimilation episode may be completed and appropriate action taken without consciousness. If assimilation episodes have direct impact on our own role in the world (e.g., they are life threatening or rewarding) they are emotionally labeled and they are stored in the neural machinery of the hippocampus for later more detailed processing. During sleep these stored representations of past events are consolidated in memory. Our recent analysis points at periods around spindles in light sleep as times when MSRC is open for small changes that may also involve significant changes of existing internal models of the world. Events that may require fairly significant changes of our self-image may require many nights of sleep to be “accommodated”. Very dramatic events or recurring ones may be impossible to accommodate, thus leading to pathology.

Assimilation and accommodation should be considered as poles in a continuum. Pure assimilation corresponds to robot like behavior (e.g. driving a car reacting to situations but not remembering doing it afterwards). The closest periods to pure accommodation are the brief periods during spindles, when stored information in the hippocampus and amygdalae is transferred to a more permanent store in the cortex; during these periods the MSRC is briefly open to change. For much of the time brain activity is a mixture of assimilation and accommodation; accommodation-like memory consolidation of recent events may proceed during quiet periods in the awake state provided they involve minimal changes of neural circuits and practically no change in the internal model of ourselves. For these periods, when assimilation and accommodation is not cleanly separated it is best to think in terms of the ZPD, originally defined as the difference between what a learner can do with guidance from a teacher or with more capable peers, beyond what he can do alone [19]. For our purposes, we define ZPD as what the existing neural networks can do but have not done so yet; in principle actions in the ZPD are likely to require no change in the basic networks and specifically no change in the MSRC. Fig. 1 gives a schematic of how the ZPD relates to routine daily operations.

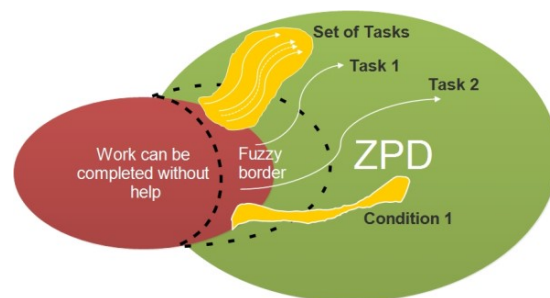


Fig. 1 A representation of the ZPD as it is originally defined (green area). The same representation is valid for our definition which also adds the (implicit in earlier works) comfort zone (CZ) as described in the text.

The current state and past history of the neural networks of an individual define two zones. The comfort zone (CZ) corresponds to states that can be reached routinely (through assimilation) and hence corresponds to work/tasks that can be completed without any outside help (red area of Fig.1).

Around the CZ exists a wider range of states that is potentially reachable by existing networks without any need for substantial changes in the structure of these networks (green area of Fig.1) but they are usually unreachable without help from a teacher. The border between the two areas changes during accommodation and at any one time is not firmly defined; it is represented by a “fuzzy border” in Fig. 1. An example of activity in the fuzzy border is a motor skill (like riding a bicycle) that was learned many years past. It is a skill apparently forgotten, but quickly coming back after brief use.

D. Play and dreams in the ZPD

For millennia learning was accomplished through play [20]. In our framework play is seen as an excursion into the ZPD, guided by forced choices for action. Vygotsky himself pointed out that, in a game situation, a child performs ahead of its current capabilities within what he called the ZPD.

In reference [9], it was suggested that during NREM sleep memory consolidation modifies neural networks, first during light sleep by adding what is stored during the previous day(s). The process continues during deep sleep, where the neural networks that have been augmented are trimmed. At the times where the neural networks are accommodated (in NREM2) and trimmed, MSRC is also open to change, but only after the areas responsible for monitoring the environment are inhibited and the input from the senses is blocked. This ensures that the MSRC is minimally interfered with, changed only as much as needed by the new memories. This ensures that the genetic endowment as shaped by the early years in life is preserved and that the self (MSRC) in the morning is the same as the self of the previous morning, in fact more so than the self of the previous night. The memory consolidation and minimal changes of MSRC during light and deep sleep reshape the ZPD; the activity of the MSRC reaches a crescendo during REM [7], which we interpret to be the play in the reshaped ZPD, when the self also participates, as a preparation for the activities of the next day and the further memory consolidation that may follow in the next cycles through the sleep stages [9].

III. NEUROFEEDBACK WITHIN THE GENERALIZED FRAMEWORK

The new framework, as described so far, provides a unified description of learning during awake state and sleep [9]. The same large neural networks with key nodes at specific brain areas operate during the day and evening. During the day, they manage interactions with the physical and social environment and accumulate memories of salient encounters for later consolidation. During the evening, these memories are consolidated allowing some changes in the MSRC. The monitoring of the internal milieu and the external environment is managed by the saliency system with key nodes at the right insula and the rostral anterior cingulate cortex. Attention prioritizes external events for temporal storage in the hippocampus during the day and memories from the hippocampus for more distributed and permanent storage in the

cortical mantle during sleep; in both cases what is to be stored is sharpened by activity in the basal forebrain [9].

The new framework provides a common language for exchanges between specialists from different disciplines with common core the standard model of modern neuroscience. Its usage has so far been described for learning and education [21] and NF [9]. We will focus for the remainder of this document on EEG NF that is using features of the EEG as they are recorded to guide brain activity into more physiological patterns of activity. This can be done either by presenting an analogue of the activity to be changed (e.g. the spectral power of alpha band in a dial or linear scale) and asking the subject to keep it high. An alternative EEG NF approach relies on behavioral psychology techniques namely positive and negative reinforcement. The subject observes or becomes engaged with a video; what the subject sees and hears is modified in such a way that changes in the EEG in the good (bad) direction are rewarded (punished) by making the audio and/or visual stream more pleasant (unpleasant).

EEG NF has been around for half a century. An uneasy peace between skeptics about EEG NF and its practitioners has erupted to heated debate recently [22, 23]. The uneasy peace prevailed for decades because the two communities did not interact much. In the last couple of decades the claims of NF grew and some supporting evidence arrived from other NF modalities, notably fMRI and MEG [5]. This state of affairs demanded more thorough investigations that when they were performed brought some support but a lot more negative evidence [24]. Some new directions for advancing this debate forward are discussed in reference [9]. The starting point is how NF is seen under the new framework. NF is viewed as an intervention that allows a controlled modification of the core representation of self, i.e. the MSRC. Seen from this point of view, NF together with any other learning experience, are seen as incomplete interventions, relying on the natural processes of accommodation during sleep to complete the slight change of the MSRC to a “normal” state, i.e. a state that is compatible with the current model of the world [9]. The prediction then is, that the modification of the MSRC (by neurofeedback plus sleep) will lead to changes in the ZPD. The following sections discuss how the effectiveness of any such intervention can be objectively evaluated by computing differences in task-related trajectories in the old and new ZPDs. Early results will show examples where such quantitative changes are identified in the context of a NF intervention for smoking cessation.

IV. EVALUATION OF EFFICACY OF INTERVENTIONS

In Fig.1 trajectories are drawn corresponding to traversals of CZ and ZPD corresponding to a task, a set of tasks, and resting states (e.g. relaxing with eyes closed, fixating on a spot on a screen, listening to a specific piece of music etc.). A measure of the current normal physiological range of brain activity (n-PRoBA) can be defined objectively for each such path from measurements of the raw EEG, MEG, fMRI or any other objective correlate of brain activity. In each case the n-PRoBA is a quantitative description of these traversals, under the lens of the specific instrument used and for the specific

task(s) or resting state(s) employed. The plurality of tasks and instruments that can be used and the variability of the EEG/MEG/fMRI measures from subject to subject and even within a subject at different times diminish the usefulness of any such n-PRoBA measurements. We get closer to a useful measure if we adopt as n-PRoBA measures, the actual brain activity extracted from the data, i.e. if we move from signal space to source space n-PRoBA. Even for this case however the usefulness is limited because the within and across subject variability is still very high.

The following approach can provide a useful measure of the difference in paths in the CZ and ZPD: The source space n-PRoBA are extracted for a set of resting state measurements twice; once before and the other after a standardized set of tasks. Thus, a complete n-PRoBA session will be composed of (a) Resting state condition(s) before (bef-T), (b) Active Tasks/conditions and (c) Resting state conditions after (aft-T). Two complete n-PRoBA sessions are performed one before and one after intervention, bef-I and aft-I respectively. The path differences before and after “sense” changes due to either Task or Intervention in the ZPD of the resting state. Tasks are selected to amplify ZPD changes and allow second order differences to be defined (see below). An n-PRoBA is prefixed by its modality, e.g. EEG-n-PRoBA, if EEG is used.

A. First order n-PRoBA contrasts

Consider the following first order contrasts:

$$\Delta^{\text{exp}} = \Delta^{\text{exp}}(\text{n-PRoBA}[C1], \text{n-PRoBA}[C2]; \text{Tasks}; \text{method}) \quad (1)$$

$$\Delta^{\text{c}} = \Delta^{\text{c}}(\text{n-PRoBA}[\text{bef}], \text{n-PRoBA}[\text{aft}]; \text{Tasks}; \text{method}) \quad (2)$$

A gross measure of the patch of CZ and ZPD is provided by (1); it is defined by method: simple difference, statistics, connectivity etc. and two resting conditions (e.g. C1=eyes open and C2=eyes closed) for either the period before (exp: before) or after (exp: after) the active task. In (2) the comparison (method defined as above) is between two identical resting conditions (same C-type) one for the period before and the other for the period after (Tasks or Interventions).

These first order comparisons provide an objective measure of the n-PRoBA differential of ZPD landscape for the Task(s) employed. Although much detail is missing from the cumbersome definitions of (1) and (2), we will simplify the notation further, as much as keeping the meaning clear allows.

B. Zeroth and Higher order n-PRoBA contrasts

The methodology defined above includes the usual case of comparing resting states before and after interventions, without any intervening tasks. These zeroth order comparisons can be described under Eq. 2, with tasks replaced by interventions and (bef) and (aft) referring to before and after the intervention itself (bef-I and aft-I). The formalism can also be used for experiments where there is neither intervening task nor intervention but the comparison is between resting (or even active) states for two different populations, e.g. disease and control, or, two types of developmental disorders. The process can be elaborated in the opposite direction defining

second order differentials. A second order differential can be defined by contrasting the results of Eq. 1, i.e. comparing before and after the intervening tasks, using as input the first order mapping of ZPD obtained by contrasting two conditions. Alternatively, we can compute the contrast between the results of Eq.2, i.e. comparing the first order contrasts of the same condition before and after intervention comparison, computed before and after the intervening task(s). These second order differentials of n-PRoBAs can reveal ZPD changes excited by the selected intervening task(s) and resting conditions.

V. AN EXAMPLE OF EFFICACY EVALUATION IN A NF INTERVENTION FOR SMOKING CESSATION

A. Summary of the study

This final section provides examples of how the general framework is applied in the NF work of our group within the project SmokeFreeBrain (SFB). The full intervention in our team’s part of the SFB protocol has twenty NF sessions, divided into two parts. In the first part, five NF sessions were delivered over a period of 2.5-3 weeks, using the Othmer Infra Low Frequency (ILF) protocol [25]. In the second part, 15 more NF sessions were delivered using the alpha-theta (α - θ) protocol [26, 27] over a period of about 10 weeks. Within the broad structure of the 5 ILF and 15 α - θ NF sessions, and in line with the general framework, we have adopted a personalized approach, adjusting the details of each one of the individual NF sessions to fit optimally the needs of each specific individual. The usual way of evaluation of the effectiveness of NF sessions is in terms of the actual outcome (smoking cessation) and measures of craving, dependence and other psychological factors gleaned from questionnaires. This will also be followed in our study; in addition, we will use the analysis of section (IV) to follow changes in resting state activity over the NF sessions. To this end we record three more EEG-n-PROBA sessions, one before the first NF session, one soon after the first part (5 ILF NF sessions) is completed and before the next part begins, and the last one after the full 20 NF sessions are delivered. The three EEG-n-PROBA sessions are identical, consisting of three resting state tasks (Eyes Closed (EC), Eyes Open (EO) and Eyes Fixating (EF)) delivered in exactly the same way before and after the Active period in between. The active period is composed of music listening and a text reading sessions. About 30, artefact free 30 second-long periods of EEG are selected for analysis from the period before the Active part and the same number of segments from the period after. The EEG data of each time slice of data are analysed tomographically using an EEG adaptation of magnetic field tomography (MFT) method [28, 29]. The spectra for each voxel in the brain are then computed for each of the 30 independent samples. For each voxel the spectral power over a period of 3.2 Hz frequency band, sampled every 0.2 Hz. Thus each distribution is composed of 510 (30x17) points. The t-test is used to compare the distributions of spectral powers, between conditions, i.e. like Eq. 1, or for the same condition for the sessions before and after the active task, i.e. like Eq. 2. These comparisons yield

highly statistically significant changes, typically with $p < 10^{-8}$ (after the conservative Bonferroni correction).

It is stressed that the purpose of the examples are to demonstrate how the differentials of n-PRoBAs can be used to provide detailed information about changes across interventions, that have remarkable stability for individual subjects, and they are identified with extremely high significance. It is beyond the scope of this paper to describe specific results in any detail, partly because the space is not available and partly because the study is ongoing.

B. Stability of highly significant n-PRoBA differentials

Fig. 2 shows the first order comparison between conditions for four separate periods. The results demonstrate that these differences are highly significant and stable, at least over the first five NF sessions.

C. Changes in individual conditions

Figures 3 and 4 shows highly significant changes ($p < 10^{-8}$) for each condition, in the alpha and gamma bands respectively. In the alpha band the most noticeable difference is seen in the EC condition. There is no highly significant change in the differential of the EC condition between the tasks for the initial EEG measurements recorded before the start of the NF sessions. By the end of the 20 NF sessions the spectral power in the alpha band during EC is much stronger after the active session than before. The changes are widespread and they resemble the differences seen in Fig. 2, between EC and EO conditions. A possible explanation is that NF helped the subject to relax more easily with eyes closed in general.

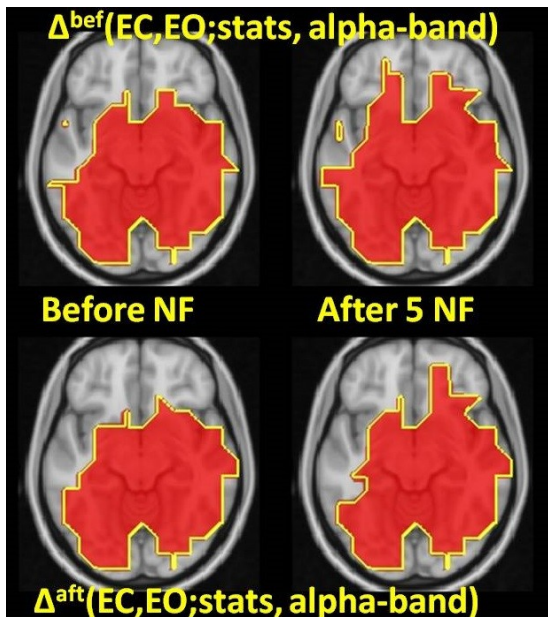


Fig. 2. EC vs EO comparisons before (upper row) and after (lower row) the active Tasks from data before any NF (left column) and after the 5 ILF NF sessions (right column). For this figure, condition 1 is EC and condition 2 is EO. In this and all figures that follow, red (blue) areas with yellow (mauve) boundary are brain areas where the spectral power is higher (lower) for the first than that the second distribution at statistical significance $p < 10^{-8}$.

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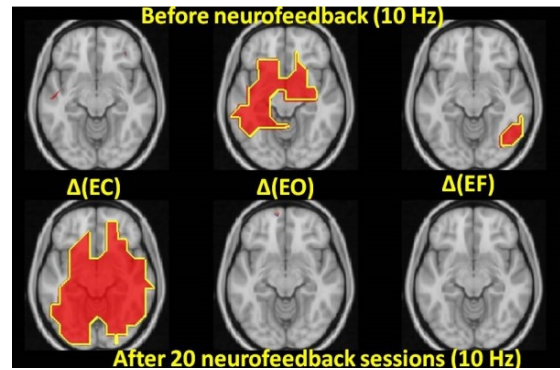


Fig. 3. The statistical comparison between the spectral power in the alpha band, after versus before the active task, shown separately for each condition (EC, EO and EF from left to right). The results are displayed for the measurements before any NF (upper row) and after the completion of the 20 NF sessions (lower row)

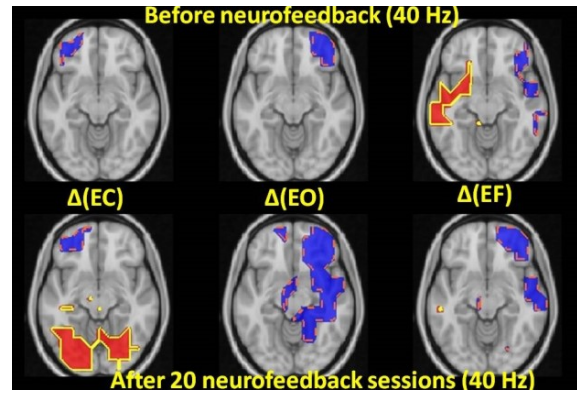


Fig. 4: The same conventions as in Fig. 3 but for gamma band (35 – 45 Hz).

Before NF started, the small change introduced by the task could not stand out from the large variation present in the EC condition before the intervening tasks. After the protocol was completed, the subject enters the first EC condition in a stable and relaxed condition; the intervening tasks is stressing the brain a little and the enhancement of the “idling” alpha rhythm that results is sufficient to produce highly significant change. However, the increases in alpha power in the EC condition are accompanied by gamma band increases in the second session suggesting that NF also changed the processing of the intervening task or the way the system relaxes after the completion of the task in the second EC period.

E. Limitations and other details

The goal of this work is not to describe results in any detail; we show results for only one subject and in only one axial cut (where changes in the resting conditions are expected). Also, to fully interpret the results, the EEG of the intervening active session must be analysed too. Therefore, with the above decisions we lost important information and interesting and important details are not displayed. The decisions did however allowed some continuity in the results and allow the reader to compare them in the background of the fixed anatomy. Also, within the limited space available, the results demonstrate that differences in spectral power of resting state conditions have robust spectral properties that are stable on either side of an active intervening session (Fig. 2). Comparisons of spectral power of the same condition before and after the intervening session show highly statistically significant changes that can be modified by the 20 NF sessions (Figs. 3 and 4). The results reported are from a female subject who was a moderate smoker before starting the NF sessions. She attempted and succeeded to stop smoking just before the start of the NF sessions. She continued to refrain from smoking throughout the NF sessions and she has not smoked in the six months after completing the 20 session NF program of SFB.

VI. CONCLUSIONS

A general framework for learning that encompasses interventions like NF was summarised. Early results were presented demonstrating how this generalised framework can be used operationally to define quantitative measures for the evaluation of NF efficacy. These measures can then be related to the main outcome (smoking cessation) and to measures of changes in craving and dependency (extracted from questionnaires and/or behaviour) or more directly from measures of smoking related substances in saliva, urine or blood. Definitive results are forthcoming; for now, enough data have been analysed to suggest that n-PRoBA differentials correlate with changes in specific brain areas that are consistent with what other studies on smoking cessation have found. We also have strong indications that specific regional changes in n-PRoBA differentials correlate with dependency and craving measures derived from questionnaires [30, 31].

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