Neurofeedback Using the Phenotype and Z-Score Modalities

Cynthia Kerson, PhD, Jay Gunkelman, QEEGD, Tom Collura, PhD

Medicine is an art—And the State of this Art Uses the Widest Pallet

This article was created because we (Cynthia, Jay, and Tom) found ourselves in dialog at AAPB regarding the appropriate use of the many forms of Neurofeedback currently available to clinicians. I suggested Jay and Tom answer a few questions regarding their specific approaches to help those of us in "the trenches" decide how each modality/philosophy can be applied for a given client/population. Jay Gunkelman has developed the model of phenotypes and Tom Collura, along with Robert Thatcher has developed the Z-score training methodology. Please find below three questions that the author presented to Jay and Tom and their respective responses. I hope this helps you to decide on water color, oil, or gouache.

What do you find to be the distinguishing features of the z-score and phenotype neurofeedback training methods?

TOM: All QEEG-based training including Z-score training needs to follow the guidelines:

- There needs to be a clinical complaint. *(Jay adds: we discussed a less clinical orientation for this section)*
- There needs to be an EEG abnormality that is consistent with the complaint.
- There needs to be reason to expect that reducing the EEG abnormality will alleviate the complaint.

Then you proceed with training relative to the EEG abnormalities. This rule applies to ALL QEEG-based treatment, not just z-scores. I have seen QEEG-based protocols that do not follow these guidelines that have adverse (or mediocre [ED]) results. For example, if right frontal beta is "low" then training it up is definitely not a good idea. As another example, someone with chronic anxiety who exhibits a diffuse alpha excess as a coping mechanism, does not want that trained down.

With live z-scores, you can also see cases where the live "training to the norm" is not indicated. For example, excess C4 SMR may be a "peak performance" signature that should not be trained down. Similarly, left hemispheric hypocoherence may reflect superior language ability (I have seen it in public speakers, professors, etc). You don't want to train that either.

However, when you see a clear sign of an abnormality related to a complaint QEEG-based protocols, including live z-score training, are indicated.

Finally, it is also clear that using a phenotype-based approach and basing protocols on the phenotypes offers an additional, highly robust way to get around the above considerations, when the QEEG does not yield to a simple "you need to fix this" type of analysis.

Live Z-score training is particularly valuable for connectivity training in which it is difficult to establish appropriate targets. It has the capability of targeting multiple connectivity metrics simultaneously toward normal, allowing the brain to normalize in an extensive and comprehensive fashion, with an observed minimum of sessions. If used in a simple "train to the norm" manner, it can be extremely effective in many cases. Dick Stark, MD, a clinician in Florida, has been using Z-score extensively in his practice. When I asked him about this, he responded, "The z-scores we use are dynamic, and provide information unavailable when using a static Q." He is learning to watch the dynamics of the brain in action, which is unique to live z-scores. However, there may be observed EEG deviations that, for certain reasons, are not desirable to normalize. These include some "peak performance" characteristics, as well as various compensation or coping mechanisms, whose normalization does not comprise the most optimal therapeutic path. One of its strengths it that it addresses the EEG deviations directly, without having to resort to categorization. Another is that it can lead to new insights gained by the direct observation of a system of real-time metrics revealing underlying dynamics and organization. The orientation of live z-scores is neutral, in that once the normative criteria have been establish, it endeavors to reveal the EEG parameters and their underlying dynamics, without predisposition or bias with regard to what can be discovered.

The Phenotype approach has the benefit of using physiological and clinical insight to categorize observed EEG characteristics in a functional way. It can lead to effective protocols that would not be suggested by merely observing QEEG deviations and seeking to normalize them. It produces protocol recommendations that tend to be standardized, and attempt to address an underlying condition, by providing an appropriate functional challenge in the particular recommended training. In this regard, it has more of an "Eastern," yet entirely scientific, orientation. It has a weakness when confronted with complex QEEG circumstances that can be more effectively targeted automatically using live Z-scores. It is also limited to the fixed number of preconceived phenotypes, and is thus more restrictive in its application. *(Jay adds: these statements need to be substantiated).* It should be considered as an essential component of any evaluation, as a means of understanding the "sanity" of the overall assessment, and to guide the choice

of training protocol, which could be any of a wide range of types.

The two methods differ in their level of granularity. Whereas phenotypes must fall into a finite number of categories, which are comprehensible to the human interpreter, Live Z-scores display an unrestricted range, as patterns emerge from the myriads of "red and blue numbers" that can form structured patterns on the screen. Dick Stark has learned to read these patterns. This granularity can translate into training power, particularly in the case of many varied connectivity deviations. Even in the face of a daunting "spaghetti head" configuration, live z-score training can effectively train away essentially all of the deviations in a relatively small number of sessions (less than 25 in the examples cited elsewhere in this and the last issue). Whereas a phenotype might classify a broad range of such situations as "epileptiform," live z-scores are capable of teasing out multiple connections and deviations, to provide a very precise targeting strategy.

I agree strongly with Jay's comments (below) regarding the importance of a multivariate analysis. Indeed, live z-scores can provide a foundation for further development of targeted protocols that exploit physiological insight and clinical guidance, as both z-scores and phenotypes become more fully developed, and more fully complimentary.

JAY: The Z-score training's orientation to the mean of the EEG metrics is a different orientation than we use with the phenotype approach. There are a limited number of phenotypes, and they cut across the DSM categories, but unlike the DSM, the phenotypes predict effective therapy approaches, both with medication, as well as with NF.

I conceived the classification system for EEG in the late 1990s, and it was written up in 2005 based on retrospective experience with EEG analysis. This system has since been tested for medication prediction in ADHD. In ADHD only one phenotype has a positive response to stimulant medication (the frontal slow phenotype). The phenotype approach has also been used for addiction with great success, and those outcomes (N=30) will be presented this fall at ISNR, with the phenotypes suggesting the bulk of addiction being driven by two different physiological systems (over-arousal, and cingulate drive).

In phenotypes the client's EEG findings are matched with the phenotypical patterns that comprise the preponderance of the variance in the EEG. The phenotype(s) identified will be a cluster of data points that are *not at the mean*, but rather data points that are divergent from the mean. In the phenotype approach, each phenotype divergence has known generators and distribution pathways. These are all well-characterized in the IFCN's (International Federation of Clinical Neurophysiology) position paper on EEG rhythm generators, and has prescribed interventions that will move the divergence back to it's phenotypical mode. . . which is not at the group mean, but characterizes the stable (though divergent) base-state for that phenotype.

To become clinically normal, an individual does not need to have "normal" (oriented to the mean) EEG values, but rather simply needs to regress to the mode of the phenotype, since the **phenotypes are also present in the normal population.** "Normative" databases account for the divergence of these groups or clusters from the mean by increasing the variance of the data set, rather than creating cluster based modal subsets of the clinically normal individuals.

I will be showing the incidence of the phenotypes in the ADHD and also in the "normal" population at the ISNR meeting in August as well. The data suggests that "normal" is not a difference in kind from the clinical population, but merely a matter of dimensional divergence distance. Normal health brain function does not reside at the statistical mean, and exceptional states are definitely not a function of having EEG values residing at the group average.

I would propose that for pathological divergence, regression to the mean would be an improvement... but for peak performance applications, average or mean oriented results simply do not make sense.

In our work, we have shown that returning people to their phenotypical modes, and reducing their divergence creates clinical improvements, but we also are showing phenomenal gains in neuropsych function, which look like peak performance training, not just removing their specific complaint.

We treat all people who present to us, whether for peak performance or for a clinical complaint with the same overall approach, which is a customized assessment for phenotypes, and the individualized though standardized set of NF or medication approaches. The diagnosis or behavioral complaint does not direct therapy, though it is taken into account when prioritizing phenotype approaches when there are more than one (which is common).

The inter-rater reliability of the phenotype evaluation is quite acceptable with lambda values of 0.90 and better without specific training of the raters in identifying the patterns. The classification is simple and reliable.

Though we have tried to objectify our approach through publication of the phenotypes and their predicted interventions, and are actively doing prospective replication of the outcomes, I will not be satisfied until we can get the classifications performed by a computer algorithm, and our group and others are actively working on or discussing this automation.

I am happy to see new approaches developed, such as Z-score training, which does hold great promise for some applications, though as an emerging new tool, it remains for the clinical community to use the tool and identify the strengths and weaknesses of this emerging application. I understand the excitement of a new tool, but I also know that we should attempt much and claim little, until the published outcomes support the experimental application.

In an anxious individual, various EEG findings can correlate with the anxiety, from frontal hypoperfusion (seen as alpha and/or theta), a frontal lobe asymmetry (more hypoperfusion on the right), as well as some other specific findings like cingulate involvement (over-focus on those things that make one anxious, such as seen in GAD), and even over-arousal, seen as faster alpha. If one were to normalize all these findings, not only might the anxiety be removed, but if the alpha were slowed, it may also degrade the semantic memory and IQ performance... so not everything associated with anxiety is restricted to being associated with the complaint alone... and some may be associated with optimal states due to a pattern of divergence associate with both the complaint and the peak state.

Thus, regression to the mean values does not always yield better function, and "normalizing" to a Z-score mean is not always the best course of action for all values... it can't be done blindly. . . and the field needs to identify and fully flesh out the emerging new application's strengths, as well as these potential weaknesses, so that our clients can be served with the most effective approaches possible.

In epilepsy, where we have effective NF applications (both SCP and SMR) proven in blinded placebo controlled studies, applying the new Z-score training instead of known clinical approaches requires informed consent from the client indicating

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that they choose not to do a proven training and instead choose to do an experimental application using this new tool.

It should be remembered that the brain is a multivariate system, and multivariate divergence can be highly statistically significant, *even when the individual Z-score values that make up the multivariate are not themselves divergent significantly*... so not everything that is truly significant can even seen when viewed with the lens of univariate measures that populate most databases. The phenotypical divergence within the normative population (even when pulled from a well constructed database's normative grouping) shows this effect very well.

What diagnostic tools would a clinician use to determine the phenotype pattern or EEG deviations from the norm when choosing to use either modality for training?

JAY: The pattern identification and classification into phenotypes does not require any EEG/qEEG database, as it is best drawn from the raw EEG. The EEG shows the patterns easily, as witnessed by the inter-rater reliability lambda statistic of 0.90 and better for most patterns reported in our recent study, done in cooperation with Martijn Arns, Rein Breteler and Desirée Spronk (all from Nijmegen, The Netherlands).

Basic training in EEG interpretation is needed to establish competence in visual identification of these patterns, as well as any other patterns seen in the EEG morphology. The classification is not difficult, but there are some people who have difficulty seeing spatial patterns that may find this approach to be best left in the hands of those who have already established competence in reviewing the EEG visually.

This emerging approach to the EEG interpretation was published initially in 2005, so there are few trained locations in existence at this time, though those with EEG experience will have no trouble with this classification system, even without specific training (as seen in the published study, where the two raters operated independently, and did not receive any pre-experimental training to make the ratings more reliable.

The determination of phenotype classification merely requires a trained observer and the EEG, and no additional software or device expenditure.

TOM: I would say that in any case, whether training using manually targeted variables, or live z-scores, it is important to interpret the EEG in the context of what is normally expected. Even a visual examination of a neurological EEG requires an in-depth understanding of what is expected, so that deviations, whether in the time-domain data, or in derived variables, can be identified. The phenotype approach uses a combination of functionally relevant indicators, to sort EEGs into the set of categories currently used. On the other hand, the inspection of a QEEG by observing the z-scores in and

of themselves, may suggest certain conditions, but does not require the categorization of the findings. For example, an individual may have "excessive" frontal slowing among their z-score deviations, which are in fact, phenotype #1. So this type of observation is commonly recognized, based upon experience and clinical relevance, independent of whether or not one is using a particular categorization scheme.

When the phenotype reduces to "epileptiform," the detailed coherence, phase, and asymmetry z-scores can provide invaluable new information regarding the precise connectivity issues at hand. Z-scores also provide a precise mechanism for targeting connectivity. This is not inconsistent with phenotypes; it provides an additional level of guidance. Where the recommendation might be to "normalize coherences," live z-scores provide a significant means [can we use "vehicle" or another word so we're not using "mean" in a different context?] to do precisely that.

Applying z-score training does not require training "to the norm." Rather, targets are placed in the context of the normative database, and targeting starts off with that data on hand. Live z-scores can be used in combination with conventional targets such as "increasing alpha" or "reducing fast activity", and do not conflict with them. It is also possible to "delete" certain considerations from automatically targeted training, so that z-score training can be done "while leaving absolute amplitudes alone", or "while not putting a specific limit on SMR amplitude."

Again referring to the examples shown in my article in this issue, it can be seen that the use of live targets is a particularly useful way to sort out multiple deviations and target them individually or in combination, but with a physiological and clinical rationale to support it.

What do you recommend researchers interested in phenotype and Z-score training to do to facilitate further understanding and confidence of clinicians so they use either of the modalities appropriately and properly?

TOM: My first recommendation is that researchers as well as clinicians make every effort to get training and education on these, as well as other emerging methods.

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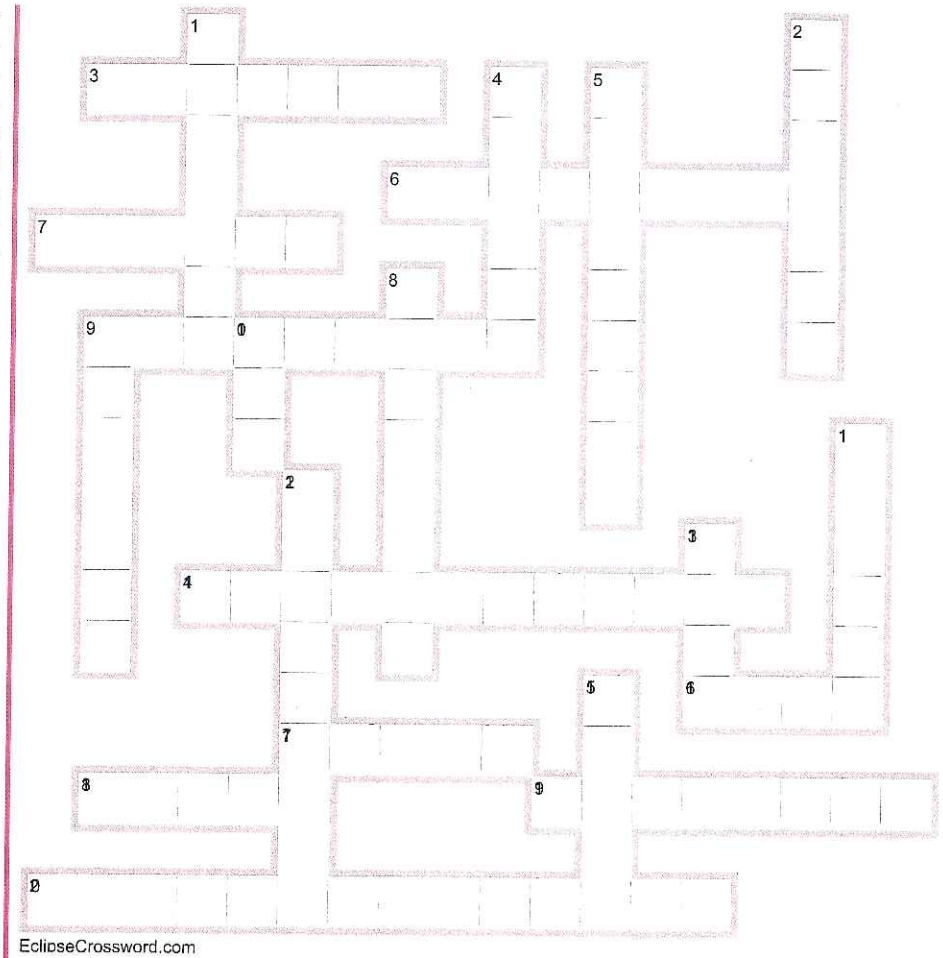

EclipseCrossword.com

Across

3. PTSD criterion D symptom
6. "Phenotype guided training" proponent
7. Alpha training pioneer
9. EMG biofeedback pioneer
14. Reduction in this seen in PTSD (two words)
16. Duty related accumulated trauma (acronym)
17. Coma training pioneer
18. Menninger clinic neurofeedback pioneer
19. activation-guided database training pioneer
20. PTSD criterion B symptom

Down

1. Symphony in the Brain author
2. Canadian AAPB neurotherapy board member
4. Lubar protege joining AAPB neurotherapy board
5. Whole brain synchrony training technique (two words)
8. Excess seen in PTSD (two words)
9. Spinal cord injury biofeedback pioneer
10. Z-score training acronym-collura
11. Mr Coherence
12. PTSD criterion C symptom
13. 12 to 35% of officers experience this
15. Lifetime Achievement Award recipient

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Nothing takes the place of direct contact with other professionals. We have had numerous experiences where attendance at a workshop or seminar, reading of a published paper, or even an ad hoc conversation, has led to fruitful work and growth for the field.

I think it is critical to avoid factionism or pedantry in forming opinions about what does or does not work, or what directions one might pursue. Often, perceived differences are actually an opportunity to learn from contrasting approaches. For example, both standard QEEG's, but particularly live Z-score technology, are important ways to bring out and quantify characteristics relevant to phenotypic classification, among other things. At the same time, even when using live Z-scores, it is beneficial to continually view the raw EEG tracings, in order to understand what is happening beneath the sea of numbers. There is only a need to make a dichotomous decision if one decides beforehand that a conflict must exist. To the seasoned, experienced practitioner, every technique brings its strengths and weaknesses to the field, and each one must be evaluated with an informed point of view.

I recommend that those who are interested contact those who are using the new techniques, and try to get a detailed, first-hand understanding of what works, when, and how. I do not recommend that we pay much attention to uninformed, negative opinions that are based upon categorical objections or hearsay.

Overall, my strongest recommendation is drawn from Buddhist wisdom, and that is to "withhold judgment," and to allow ideas to mature before taking a strong position.

I have heard categorical statements that lie somewhere between outrageous and meaningless, to the effect that "person X's approach is no good because (substitute second-hand gibberish here)." Such attitudes fail to do justice to either person X or to the speaker. It is sometimes entertaining, sometimes not, to ask the speaker exactly what they are talking about, or where they got the information. It is only when the information is first-hand, or the opinion is a considered one, that there is a chance to make mutual progress and move forward.

For my own work, I have been looking in detail at live z-scores and their use, and have also been using the phenotype approach as a way to further inform and enlighten what is seen. If both techniques are valid, as I am sure they are, then they cannot but be mutually supportive, and mutually beneficial. Again, if a live Z-score pattern suggests a known set of abnormalities such as a phenotype, and if a normalization protocol is consistent with a plan of remediation, then training to the norm is probably a good idea. In cases where the phenotype is "epileptic", then live z-scores can provide the method of choice for normalizing connectivities. In other cases, it will be more desirable to bias the training in a direction other than to the norm, or to combine the normalization with a biased component such as global power reduction, alpha enhancement, or whatever else makes sense.

JAY: The correct approach to any new tool is open minded skepticism. The phenotype approach was developed retrospectively, looking at too many years of experience and making systematic records of divergent patterns and what worked with them. This obviously has required prospective replication of the observations, and that is exactly what has been done and will continue to be done.

A study of 100 subjects and controls is just being published in the Journal of Integrative Neuroscience showing the predictive outcomes for treating ADHD with stimulants, and there is really only one of the 11 phenotypes that respond to stimulants, as predicted. Other clinical outcome predictions with phenotypes for treatment with neurotherapy for addiction (N=30) is also now being presented this Fall at the Biofeedback Society of California and at ISNR's meeting in San Antonio. Studies on Depression and phenotype prediction of medication responses are planned.

Researchers and clinicians should feel free to test the phenotype model. This is why I published the model instead of patenting the approach. I welcome tests of the model for further independent validation, as well as to help refine the predictions from the model.

I prefer the peer review and publication approach to establishing efficacy claims over promotional marketing to promote an approach, though I'm sure both approaches have their place in moving the field forward.

TOM: One thing is for sure, and that is that the EEG still contains a lot of information we have not yet begun to comprehend. It is by working on new approaches including live Z-scores, as well as phenotypic classification, that we can learn to interpret those marvelous squiggly lines, and actually use them to help people improve. Techniques that are based upon science, that use observational data, and that have a meaningful connection to neuronal dynamics, hold the most promise in my estimation.