BrainTrainUK
Changing Lives With Neurofeedback

Developmental Trauma and Applied EEG Neuroscience

Transforming Life Outcomes with EEG Brain Mapping and EEG Neurofeedback Therapy

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Executive Summary

The effects of Adverse Childhood Experiences (ACEs) and Developmental Trauma have a significant impact on the life outcomes of those affected.

Disrupted neurodevelopment is a key stage in the progression of impacts from ACEs through life to early death.

The 2013 announcement by the National Institute of Mental Health that it would be diverting research funds from the symptom-based "set of labels" of the DSM, to research that supports a new classification system, in the belief that "Mapping the cognitive, circuit, and genetic aspects of mental disorders will yield new and better targets for treatment".

One effect of this has been a surge in research into the science of the electroencephalogram (EEG), or "brainwave" signals generated by neuronal activity.

Recent techniques enable an advanced EEG brain 'mapping' process that identify neuro-markers for developmental trauma, and the use of this technique with looked-after children who have suffered ACEs is described.

We describe how our approach to neurofeedback therapy is unique in integrating the principles of Bruce Perry's "Neuro-Sequential Model of Therapeutics" by using staged modalities that replicate the normal sequential process of development.

Research has established that neurofeedback therapy is an efficacious intervention for developmental trauma. We make the case that by rebalancing neurodevelopment, the outcomes can be transformed.

We outline the business case for financing Advanced QEEG Brain Mapping and Neurofeedback Therapy, estimating a Return-on-Investment opportunity of > 20x.

We model the health economics and conduct a sensitivity analysis both on a realistic basis and under the constraints that NICE impose, and demonstrate that this intervention meets the willingness-to-pay criteria.

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Background

Adverse Childhood Experiences

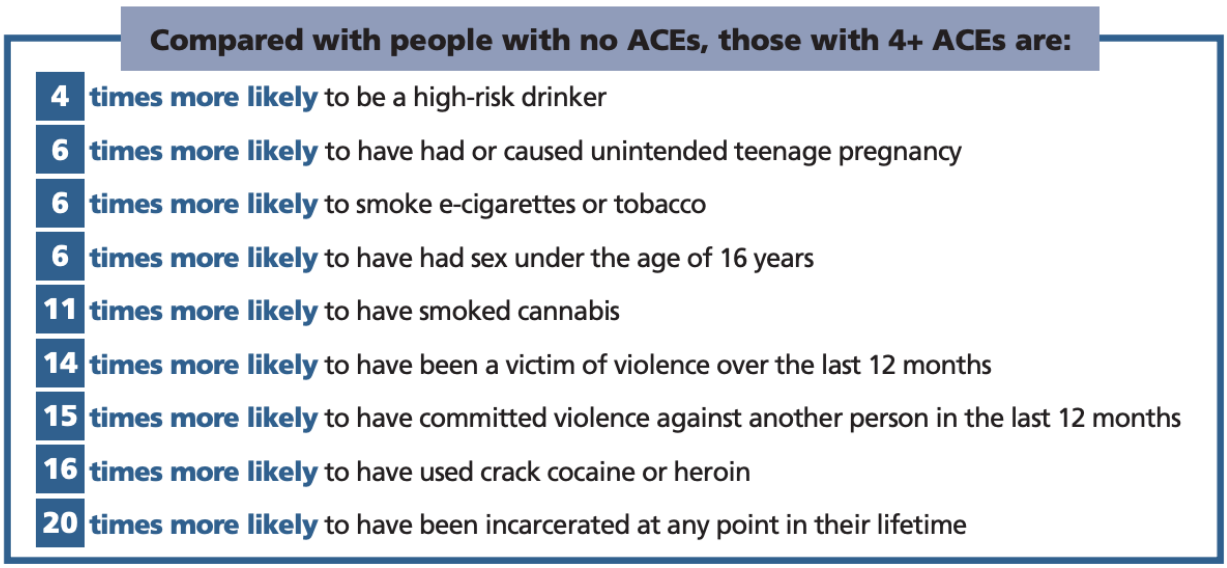
Vince Felitti at US Health insurer and provider Kaiser Permanente discovered the relationship between Adverse Childhood Experiences (ACEs) and adult health problems. In following up the drop-out rates from obesity clinics, he discovered a high proportion had been sexually abused as children, and weight gain was a strategy for self-protection[1]. Kaiser Permanente subsequently conducting the ACE Study[2] of > 17,000 participants.

The current ACE Questionnaire, identifying the experiences defined as ACEs, is replicated in Appendix A. Caution should be taken by any reader with PTSD as there is risk of re-traumatisation by reading this.

Health Issue	Risk if 0 ACEs	Increased risk with ACEs			
		1 ACE	2 ACEs	3 ACEs	4+ ACEs
Severe obesity BMI >35	5.4%	+30%	+75%	+90%	+120%
Ever attempted suicide	1.2%	+100%	+250%	+700%	+1400%
Considers self an alcoholic	2.9%	+100%	+250%	+300%	+450%
Ever injected drugs	0.3%	+65%	+360%	+660%	+1000%
Heart attack				+40%	+120%
Cancer (any)					+90%
Chronic bronchitis or emphysema		+60%	+60%	+120%	+290%

Table 1. Increased Risk of Serious Health Issues compared with Adverse Childhood Experiences[1*]

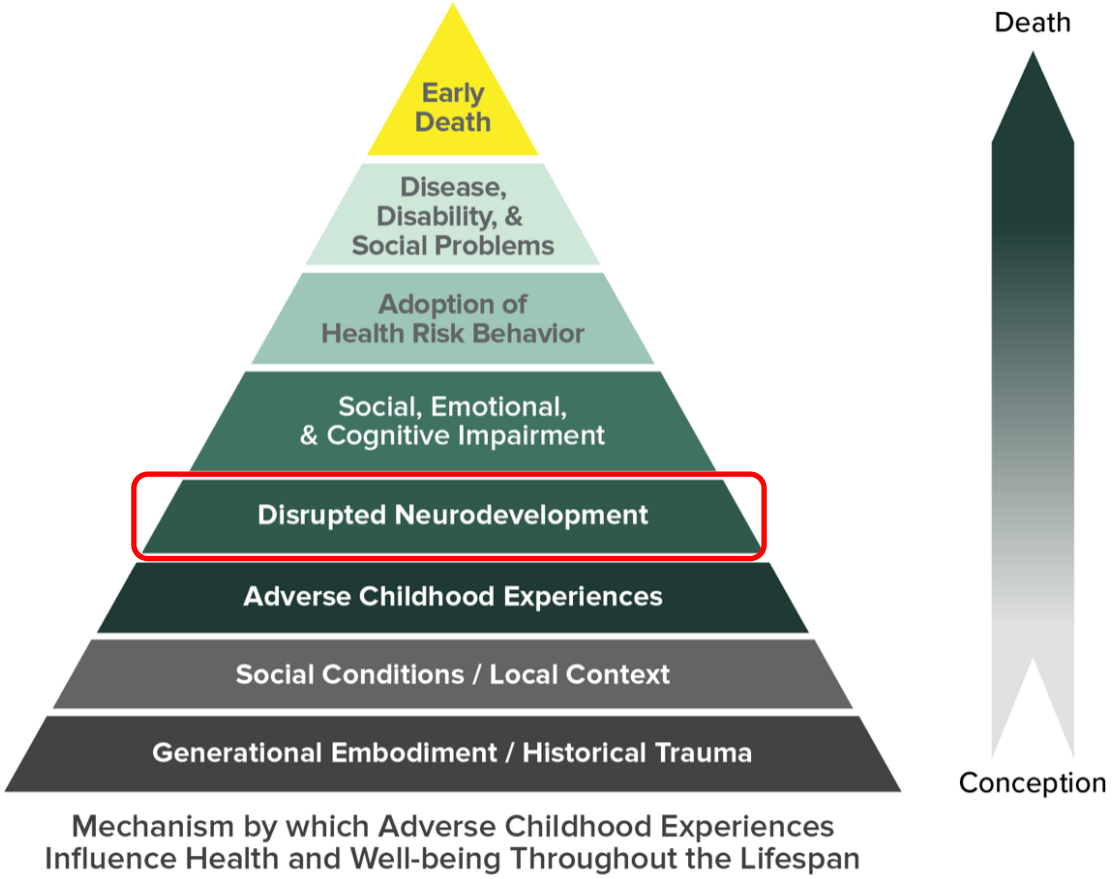
Similar research has been repeated in other areas, including England[3] and Wales[4]:



From Welsh Childhood Experiences Survey[5]

[*] Relative risk, rounded to 1-2 significant figures

The ACE Pyramid[6] illustrates how ACEs can lead to early death, and how the disrupted neurodevelopment that stems from ACEs is the cause of issues developing later in life:



Mechanism by which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

Many children experience 1 or 2 ACEs, such as divorce in the family or mental health issues, and many people are resilient enough to recover.

The evidence indicates that it is the cumulative effect of 4+ ACEs that has a multiplying effect on the risks of adverse outcomes.

Looked-after children are more likely to have experienced multiple ACEs, by definition of the Children Act threshold[7], that "A court may only make a care order or supervision order if it is satisfied that the child concerned is suffering, or is likely to suffer, ***significant harm.***"

Developmental Trauma

Developmental Trauma is the childhood version of Complex Post Traumatic Stress Disorder (PTSD).

The Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5)[8] recognises Post Traumatic Stress Disorder (PTSD).

Complex PTSD is not recognised by DSM-5, but is recognised by the NHS[9] and Mind[10] as a form of PTSD arising from multiple traumatic events.

CPTSD often results in additional emotional and physical symptoms such as difficulty regulating emotions, feelings of shame, body pains.

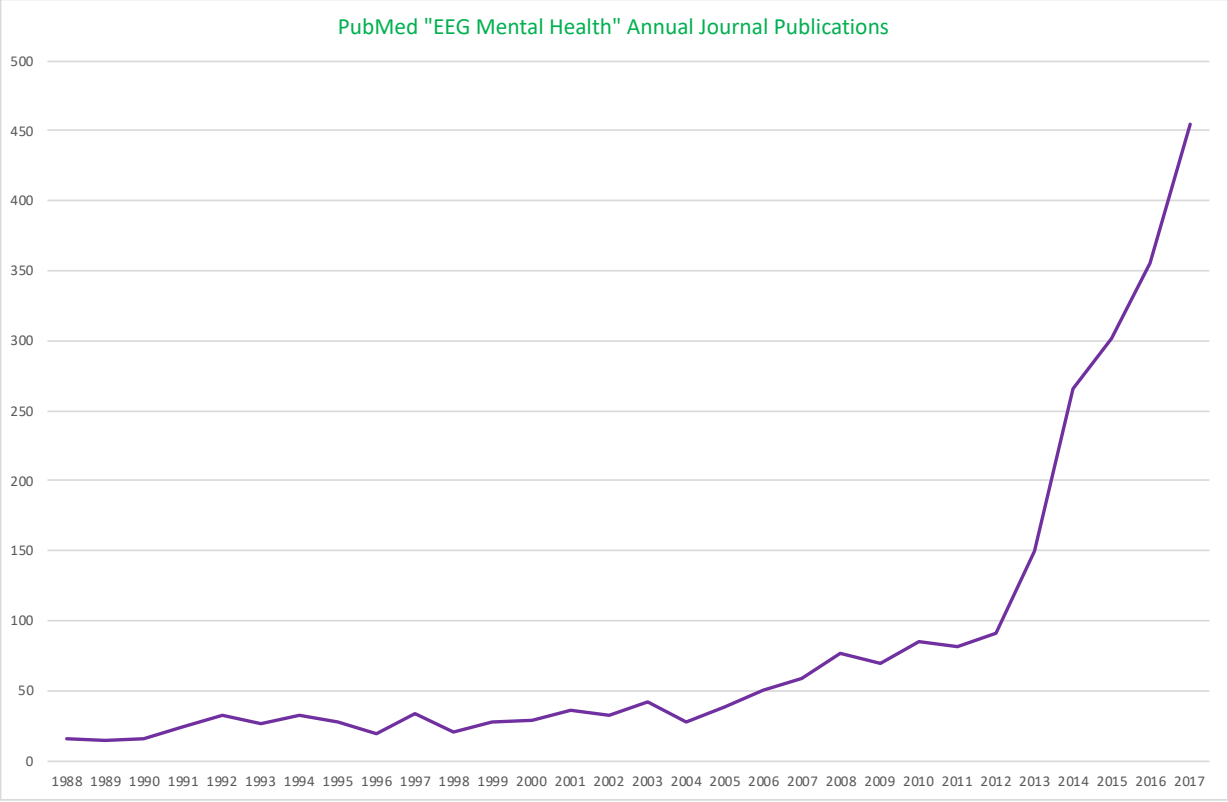
Dr Bessel van der Kolk, founder of the Trauma Center in Boston, has been instrumental in campaigning for Developmental Trauma to be recognised as a diagnosis[11]. His criticism of the current PTSD diagnosis is that it "is not developmentally sensitive and does not adequately describe the effect of exposure to trauma on the developing child."

Future of Mental Health Diagnostic Criteria & EEG

It is likely that DSM-5 will be the last of its kind. In 2013, the National Institute of Mental Health announced that it would be diverting research funds from the symptom-based "set of labels" of the DSM, to research that supports a new classification system, as "Patients with mental disorders deserve better."[12]

The belief is that "Mapping the cognitive, circuit, and genetic aspects of mental disorders will yield new and better targets for treatment".

One effect of this has been a surge in research into the science of the electroencephalogram (EEG), or "brainwave" signals generated by neuronal activity that can be measured with sensors on the scalp:



This study benefits from the increased academic focus on the application of EEG technology to mental health.

Quantified EEG Analysis

EEG analysis is an established medical technique for neurological investigations of suspected epilepsy conditions, for monitoring brain activity in Intensive Care Units (ICU) or during surgery, and supporting investigations into dementia and stroke[13].

Quantified EEG analysis also known as 'brain mapping' techniques have been available since the advent of personal computers.

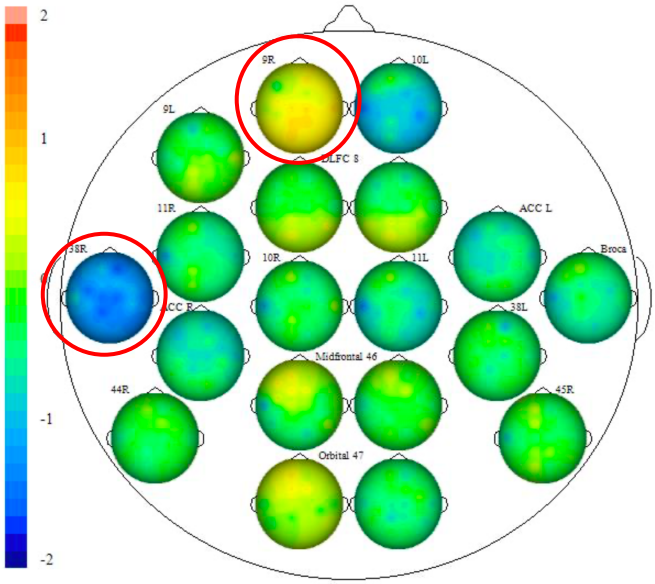
Until recently these techniques have been focused on comparing a subject's EEG patterns with those of a 'normative' database. The scientific validity of the concept of characterising an 'average' brain in this way is questionable[14, 15]. We term these 'Standard QEEG Brain Mapping'. They provide a lot of data (numbers) but lack information, analysis and insight.

More recently, techniques have evolved to identify patterns or markers within the EEG that correlate with specific traits.

In 2013 NEBA® Health[16] obtained FDA approval[17] of a device to assist with ADHD diagnosis by measuring the ratio of theta:beta brainwaves*.

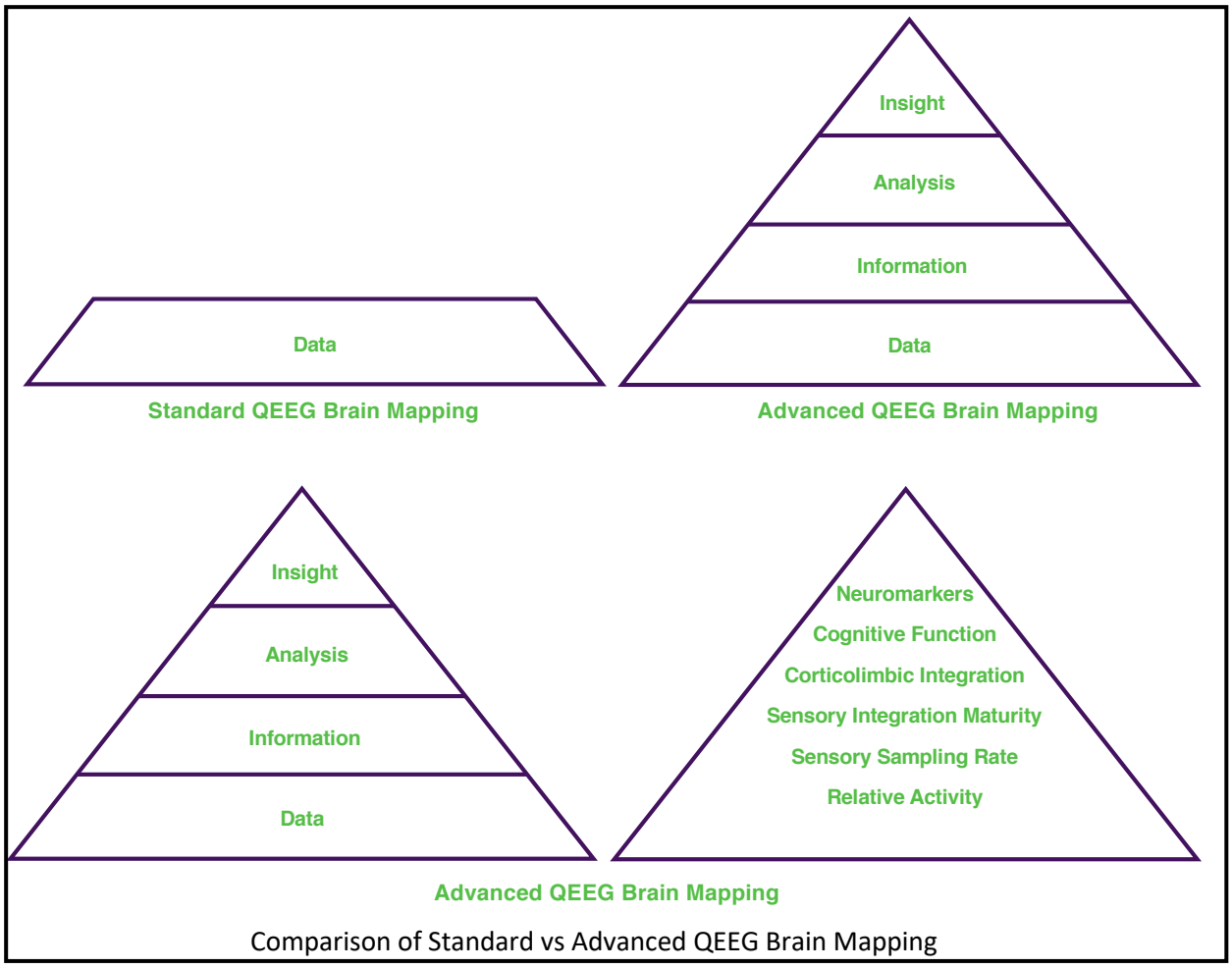
Juri Kropotov[18,19,20] in St Petersburg and David A Kaiser[21],[22] in Los Angeles have led the research efforts to establish these 'neuromarkers' for a range of traits and histories.

David A Kaiser, together Barry Sterman (see below) developed the Sterman Kaiser Imaging Labs (SKIL) software[23] in the 2000s. Neuromarkers** have been identified for multiple traits through external and empirical research, including the analysis of 'Death Row' inmates EEG patterns. This has evolved into what we term an 'Advanced QEEG Brain Mapping' capability.



**Example Neuromarkers – a participant in Surrey County Council Virtual School Project showed markers for Attachment issues and Anxiety (highlighted in red)

* EEG activity frequency bands are named after Greek letters: Delta = 1-4Hz, Theta = 4-7Hz, Alpha = 8-15Hz, Beta = 16-31Hz, Gamma = 32-40Hz. A sub-type of ADHD has been correlated with a high ratio of Theta to Beta activity.



Comparison of Standard vs Advanced QEEG Brain Mapping

Key parameters identified by Advanced QEEG Brain Mapping are patterns of **Corticolimbic Integration** measures, which are analogous to Bruce Perry's "Cortical Modulation Ratio" (CMR).

Perry describes CMR[24] as a crude estimate of the "strength" of cognitive regulatory capacity relative to the "dysregulation" of lower networks in the brain. Corticolimbic Integration has the benefit of being a measure, based on David Kaiser's Unity parameter[25], rather than an estimate.

There are a number of users of SKIL in North and South America. BrainTrainUK are the only users of SKIL to provide Advanced QEEG Brain Mapping outside these territories.

Biofeedback and EEG Biofeedback, aka Neurofeedback Therapy

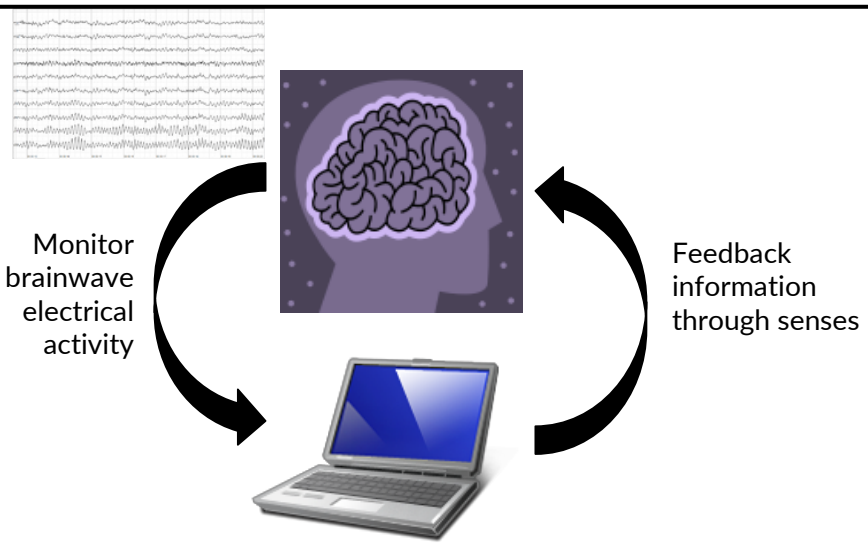
Biological feedback is essential to life, and hundreds of individual feedback systems have been identified within our bodies26, operating to regulate our internal physiology according to the established mechanisms governing those systems.

For example, in healthy individuals blood sugar levels are regulated by releasing insulin from the pancreas when blood sugar levels rise, and stopping the release of insulin when the desired level is reached.

Some aspects of our physiology we are aware of, for example our breathing or our heart-rate. But there are other aspects of our physiology including our brain's electrical activity (EEG) that we cannot observe, hear, feel, smell or taste.

Bio-feedback training creates additional external feedback loops between our physiology and the control system for that physiology (the brain and nervous system), facilitating learning, either consciously or unconsciously, to alter our physiological regulatory mechanisms[27].

EEG-Biofeedback, also known as Neurofeedback therapy or Neurotherapy, is a form of bio-feedback to improve brain regulation and function. An external feedback loop is created to take information from the brain's electrical rhythms, process it and feed it back to the brain via the senses:



Neurofeedback creates an additional external feedback loop to enable learning

This method has an estimated 10,000 practitioners in the USA[28], with clinical application to mental health disorders including anxiety, depression, attention and hyperactivity[29], neurological disorders including migraine, epilepsy, traumatic brain injury, and studies on peak performance applications[30].

Evidence Base and Development of Approach

Neurofeedback therapy for trauma has a strong evidence base from research and clinical practice.

The evidence goes back to 1989 when Dr Eugene Peniston treated alcohol-abusing Vietnam Veterans. Of 30 subjects, only 2 relapsed over a 13-month period[31].

Later studies found efficacy to address PTSD symptoms in the same population (Vietnam Veterans), for example a 1991 Peniston randomised controlled trial had a relapse rate of 100% within the control group vs. 20% in the Neurofeedback group[32].

A 2005 randomised controlled trial[33] of 120 substance-abusing inpatients at the CRI-Help residential treatment program in Los Angeles, with double-blinded outcome measures, showed that the experimental group achieved an abstinence rate of 77% compared to 44% for the controls, at 12 months.

In 2016 a randomised controlled trial was published concluding that neurofeedback therapy produced significant symptom improvement in individuals with chronic PTSD[34].

Dr Bessel van der Kolk, co-author of this study and founder of the Trauma Center in Boston, MA, says:

"In our neurofeedback lab we see individuals with long histories of traumatic stress who have only partially responded to existing treatments. Their qEEGs (Brain Maps) show a variety of different patterns.

Often there is excessive activity in the fear center of the brain. This means that their hyper aroused emotional brains dominate their mental life. Our research showed that calming the fear center decreases trauma-based problems and improves executive functioning.

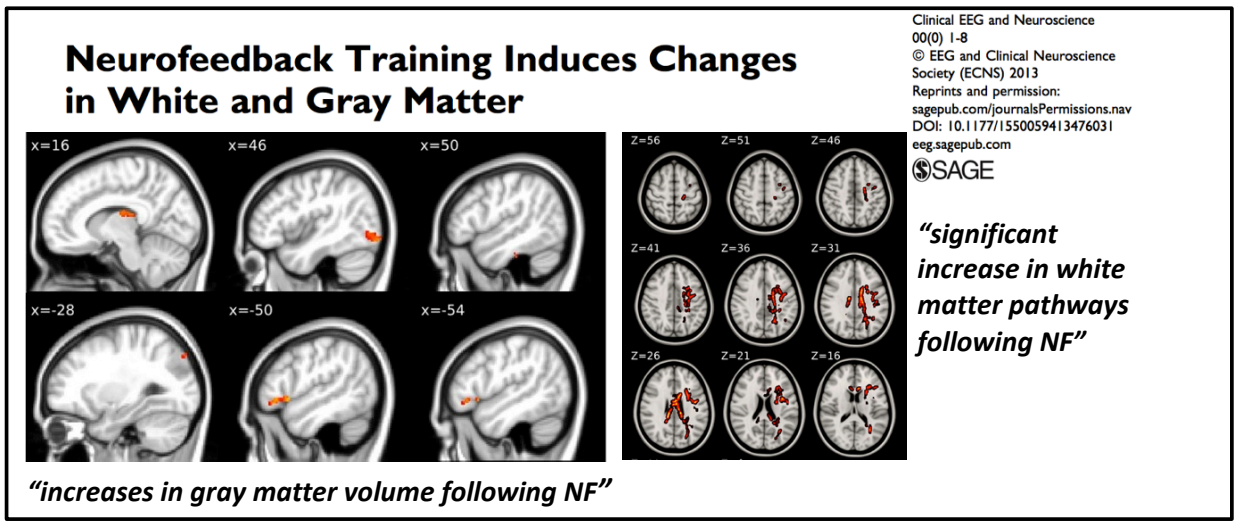
This is reflected not only in a significant decrease in patients' PTSD scores but also improved mental clarity and an increased ability to regulate how upset they became in response to relatively minor provocations."[35]

Although there is always a desire for more studies, larger studies and more blinded studies[36], the placebo question was answered a long time ago. Neurofeedback therapy was discovered serendipitously by Barry Sterman through possibly the ultimate placebo-controlled, fully-blinded experiment.

This is described in detail in Appendix B.

Since Sterman's discovery, the field of Neurotherapy has evolved.

Studies have demonstrated the physiological effects of neurofeedback, in terms of increasing grey-matter volume and white-matter tracts pathways[37]:

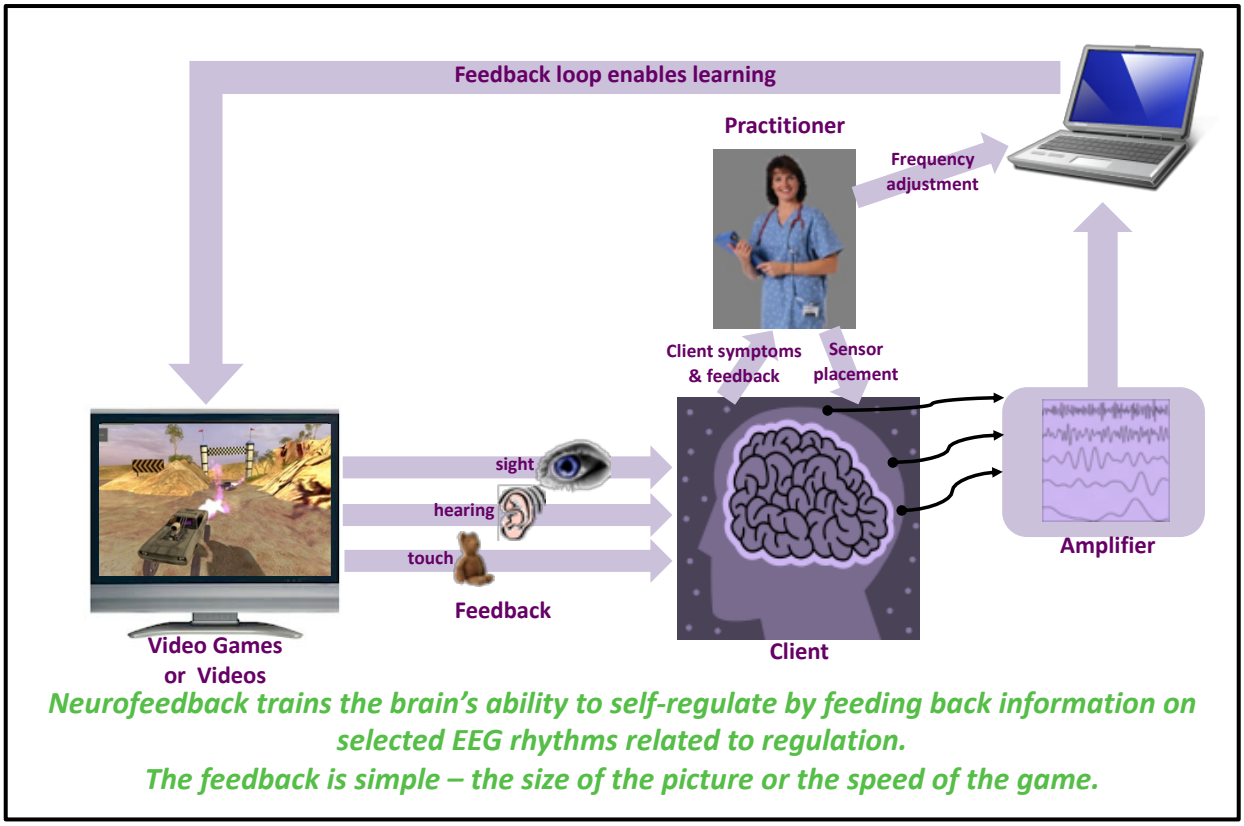


The field has developed from the beginnings where 'one size fits all' directive approaches were the standard, where all subjects presented the same way and all those in the experimental group were subject to the same experimental design.

Non-directive methods have emerged that target hubs of the brain's primary regulatory networks, focused on very low frequencies that have shown training effects in a single session in functional MRI [fMRI]-based neurofeedback studies[38,39].

Unlike the early animal research, the senses of taste and smell are not commonly used, but 3 external feedback loops are commonly established using:

- Vision (typically a computer monitor with variable speed or size as feedback)
- Hearing (variation in feedback volume level)
- Touch (using vibro-tactile feedback[40] using a vibrating cushion or soft toy)



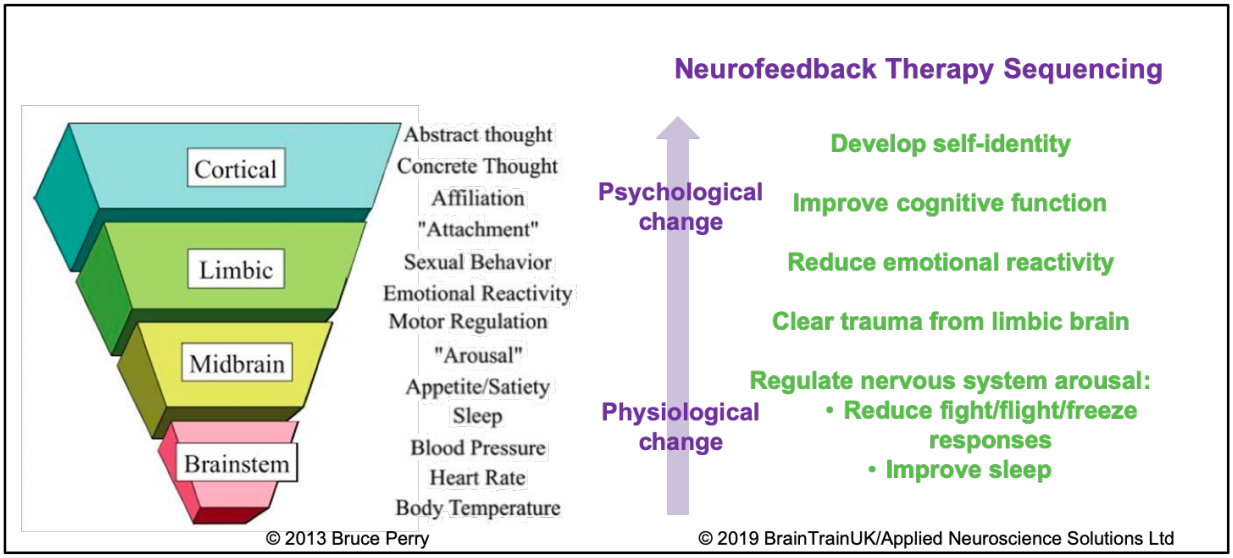
Non-directive approaches do not introduce directive processing into the external feedback loops. They present a 'pure' representation of the brain's activity back to itself via the feedback loop channels, without any concept of contingent reward, and any change is 'endogenous' or comes from within'[41].

Neuro-Sequential Model of Neurofeedback Therapy

BrainTrainUK uses multiple methods or modalities of neurofeedback therapy and has treated 100s of clients since establishment in 2013. Our approach to neurofeedback therapy is unique in following Bruce Perry's "Neuro-Sequential Model of Therapeutics"[42] by using staged modalities that replicate the normal sequential process of development.

We start with modalities that target the lowest (in the brain) undeveloped/abnormally functioning set of problems, and move sequentially up the brain as improvements are seen.

Neurofeedback therapy can be thought of as a physiological intervention that can build the scaffolding for traditional psychological interventions. We start with a focus on physiological regulation (mid-brain, limbic brain) then move onto psychological regulation (cortex), as illustrated below:



Critical Success Factors

With individualised approaches to neurofeedback, it is critical that clients/parents/carers engage in the intake assessment and planning process, and provide feedback on an ongoing basis throughout the programme. Because neurofeedback is a learning process, regularity of sessions is also critical. Although every brain is different, the rule of thumb is at least once a week, preferably more frequent, 2-3 times per week is desirable.

Another important factor that can impact the level of improvement are environmental factors within the home or school that hinder training success: an emotionally unsettled or traumatising home environment; being subjected to bullying behaviour at school, etc. In these cases the brain needs to 'survive' and there is little room for 'learning'.

Research and clinical practice tells us that there is a 15-20% subset of the population who do not respond. The reason for this is unknown, though there is speculation that dietary issues, deficits in blood glucose regulation (dysglycemia) affecting brain function, poor sleep or poor sleep hygiene can impact the learning process.

There are no current methods to predict or test responsivity in advance. Clinical experience tells us that if there is no response after 7 sessions then it is unlikely that further sessions will result in a response.

BrainTrainUK Background & Team

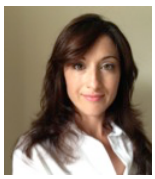
Applied Neuroscience Solutions Ltd, trading as BrainTrainUK since 2013, are the only multi-disciplinary, multi-modality neurofeedback therapy practice in the UK. We lead the UK in terms of size, geographic spread and thought leadership.

We have successfully delivered programmes of neurofeedback therapy to 100s of clients, both adults and children. We have treated many clients with a history of childhood trauma.

Surrey County Council's Virtual School contracted us to provide our services to Looked After Children, and we are in discussions with several other Local Authorities and the Adoption Support Fund to make our services more widely available.

Our team of staff and advisors include:

Zuzana Radacovska MA – Neurofeedback Practitioner
Degree in psychology, worked in juvenile justice system, BrainTrainUK practitioner for 5 years. Experience using bio and neurofeedback techniques for peak performance with athletes and executives.



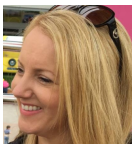
Dr Marina Chirco MD – Medical Advisor
GMC-registered NHS Medical Doctor, post-doctorate studies in Neurofeedback, Psychoneuroendocrinimmunology, Acupuncture, NAET.

Agnieszka Sosnecka MSc (Cog Neuro) – Neurofeedback Practitioner & Consultant
Cognitive Neuroscientist specialised in Clinical Psychology & Psychopathology, PhD student creativity in autism.

Jo-Anne Buttle MSc – Neurofeedback Practitioner
Educational Psychologist, MSc Educational Psychology, HCPC Registered. Extensive experience working with local authorities and private practice.

Anna Dybul MSc – Neurofeedback Practitioner
Anna has a particular interest in the use of music as a therapeutic intervention for speech disorders, and the application of Neurofeedback to peak performance.

Kirsten Antoncich MSc – Neurofeedback Practitioner
Masters in Integrative Psychotherapy, has taught English & Psychology in SEN, run a mental health service in the North East of England, and pastoral support service to schools.



Helen Wagstaff – Recruitment Consultant
Freelance recruitment professional, experience with wide range of industries and blue-chip organisations, specialist in innovative & unusual roles.

Stuart Black BSc (Eng) MSc CEng MIET – Founder & Managing Director
Chartered Engineer, 30 years experience with blue chip organisations including BAE SYSTEMS, General Dynamics, Bupa, Centrica.

Complex international product development & board-level change and interim management experience. Accountable for £multi-million P&Ls. 4 years as Executive Director at Cromwell Hospital in London. Board-level advisor to NHS Trusts.

Special Guardian to 3 children of a friend who died in 2017. Family Rights Group Kinship Panel Member & Trustee. Chair of North West Surrey Foster Care Association. Special interest in the application of EEG neuroscience to transform outcomes following Adverse Childhood Experiences,

Sairah Shah BA MA PGCE – Senior Education Consultant
Graduated in History in History (Asia and Africa) from the University of London's School of Oriental & African Studies where she also gained a Masters in History.

Sairah has taught History and been a successful education leader in a variety of mainstream contexts in including 5 secondary schools, an FE College and local authority for 20 years.

Dr David A Kaiser PhD – Scientific Advisor
Doctor in Psychology and Neuroscience. Developer of SKIL software for use in neurotherapy and brain function assessment which relies on functional connectivity and hemodynamics.

Editor of the Journal of Neurotherapy for a decade, fellow of the International Society for Neurofeedback and Research, President of the Neurofeedback Division of the Association for Applied Psychophysiology and Biofeedback, and has taught neuropsychology and neuroscience courses at various colleges. Widely published.

Marcia Saul BSc MSc – Postgraduate Researcher, Bournemouth University
BSc in Biology with Psychology, MSc in Computational Neuroscience. Marcia is conducting doctorate research defined and sponsored by BrainTrainUK into the use of neurofeedback with multiple participants (aka hyperscanning) to address social anxiety.

Dr Fred Charles BSc MSc PhD – Deputy Head of Department in Creative Technology, Bournemouth University
BSc in Computer Science, Master's degree in Computer Aided Graphical Technology Applications, PhD Computer Science.

Fred is one of Marcia's supervisors, and co-authored published research[43] on a randomised, placebo-controlled trial using neurofeedback to down-regulate limbic activity to reduce pain symptoms in fibromyalgia sufferers.

Dr Xun He BSc PhD – Senior Lecturer in Psychology, Bournemouth University
BSc in Biology, PhD in Biophysics. Xun is Marcia's other supervisor. An experimental psychologist and social neuroscientist, studying the behaviour and neural underpinnings of social attention and social perception.

Xun's main research question is how human attention and perception performance is shaped by social interactions such as joint action and shared attention, and whether social behaviour can be improved by neurofeedback? Expert in the electroencephalography (EEG) technique (including hyperscanning EEG) and Head of the Bournemouth EEG Lab.

Our Programme

Selection

Clients whose medication is stable and are able to commit to attending 2x 45 minutes appointments a week. There must also be a commitment from clients/parents/carers to engage in the intake assessment and planning process (described below), and to provide feedback on an ongoing basis throughout the programme.

There is no minimum or maximum age.

Consent, Confidentiality, Safeguarding

Initially we brief the clients on the concept, with their parents/carers present in the case of young people. If a group of young people are to take part in the programme, then this can be done as a group.

All BrainTrainUK practitioners have Disclosure and Barring Service Enhanced Checks.

Assessment

Following the briefing, each client attends our clinic individually, where the process is explained again and are told which letter code they have been assigned.

Intake paperwork is distributed to clients/parents/carers/key workers, which consists of:

- Contact details.

- An 8-page History Assessment, including sections on Personal History, Treatment History, General Development, Family History and Adverse Childhood Experience (ACE) questionnaire.

- Symptom profile capture, consisting of >150 symptoms to be reviewed, selected if the young person suffered them, and to identify 3-7 symptoms to be tracked, with a baseline rating of severity from 1 (least severe) to 10 (most severe).

A Cognitive Assessment is available for adults and children aged 6 or over. This consists of activity-based tests that are done on-line from a computer or tablet. They are provided by Creyos, formerly Cambridge Brain Sciences.

Brain Mapping

Brain Mapping is optional. If chosen, QEEG data is captured, using a suitably-sized Electro-Cap:

3 to 10-minute samples are captured, both eyes open and eyes closed.

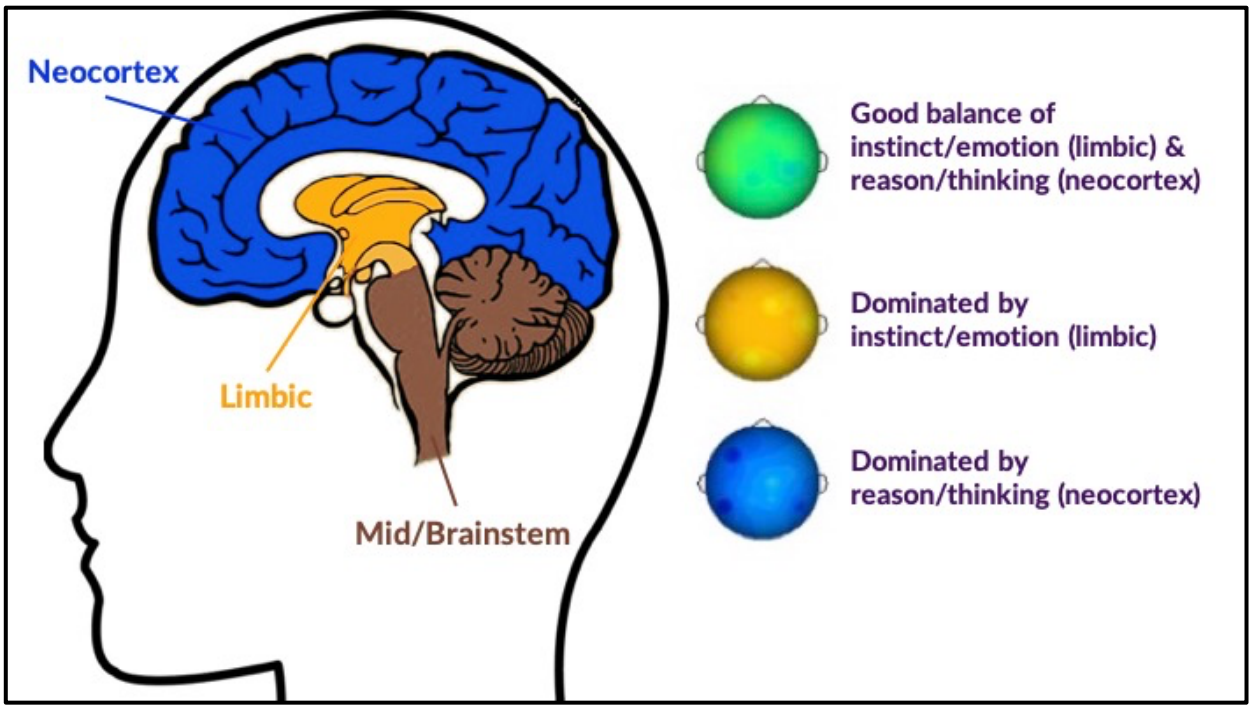
The QEEG Brain Mapping reports are prepared as illustrated by the diagram below:

AQBM reports are preferably debriefed with clients, so they can be interpreted in the context of the client. With young people this is normally done together with their parents/carers, depending on their level of understanding, and electronic copies are provided.

A key parameter measured by the AQBM is 'corticolimbic integration', which is the degree to which brain regulation is balanced between instinct (limbic brain) and reason (neo-cortex).

To communicate this concept with young people, we often use Professor Steve Peters' 2018 book, "My Hidden Chimp"[44] .

Peters uses exactly the same scientific concept with different language. Peters calls the limbic brain the red ‘chimp brain’ and the neo-cortex the blue ‘our brain’.



BrainTrainUK AQBM Corticolimbic Integration Model

We find that the neuromarkers found in the reports resonate with client’s histories and traits, for example issues with authority, being easily led (‘recruited’ in the language of the report), and anxiety.

The debriefing has several key messages and objectives:

i. Educating them the tension between their ‘own’ brain and their ‘chimp’ brain is natural and normal.
ii. Showing them evidence that the challenges that they have are reflected in their brain patterns as areas where there is an imbalance between their ‘own’ brain and the ‘chimp’ brain.
iii. Educating them that their brains are not abnormal, that their brains have adapted to working a particular way because of some of the things they have experienced, to protect them, and this is quite normal.
iv. Educating them that just as their brains have adapted so far, they can adapt again.
v. Motivating them by explaining that their past explained how they were now, but didn’t have to define their future.

The ability to back the theory up with real, individualised data has much more power than other ‘neuro-education’ activities such as using the brain ‘hand model’.

In addition, the ability to obtain insights into client's worldviews and response habits, perhaps that they themselves don't understand or appreciate, can be valuable to parents, carers, teachers, social workers and therapists.

Neurofeedback Therapy

Individual Neurofeedback training plans are created by mapping the symptoms identified to brain functions, and then to neurofeedback protocols:

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Create NeuroPlan

Symptom identification and tracking

Client Name: [redacted] **Date of Birth:** [redacted]

Description: The purpose of completing this sheet is two-fold: 1. To create a full picture of symptoms currently experienced; 2. To create the Individual Neurofeedback Plan based on these symptoms and the priority symptoms that the client wishes to focus Neurofeedback training on.

Instructions: Mark an 'x' against all symptoms that exist in the 'Symtom exists ?' column. Also mark an 'x' in the 'High priority symptom to track ?' column for between 3 and 7 symptoms. Save the spreadsheet and send to your Neurofeedback Practitioner.

Category	Symptom	Symptom exists ?	High priority symptom to track ?	Baseline rating out of 10 (for tracked symptoms)	Comments
Sleep	Bruxism (grinding teeth)				
	Difficulty maintaining sleep **	x	x	10	
	Disregulated sleep cycle	x			
	Night sweats				
	Nightmares (scary dreams often recalled) or vivid dreams	x			
	Periodic leg movements				
	Physically Restless sleep	x			
	Sleep walking	x			
	Talking during sleep	x			
	Difficulty falling asleep (physically restless)	x			
	Difficulty falling asleep (busy mind)	x			
	Diffiuclty falling asleep (fears & hypervigilance)	x			
	Difficulty waking				
	Narcolepsy (suddenly falling asleep at inappropriate times)	x			
	Night terrors (eyes frequently open, not remembered in morning)				
	Nocturnal enuresis (bedwetting)				
	Restless leg				
	Sleep apnea (pauses in breathing or instances of shallow or infrequent				

Example of Symptom identification and tracking capture sheet, showing 18/150 symptom

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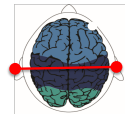
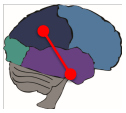
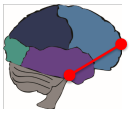
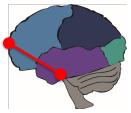
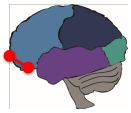
Individual Neurofeedback Plan

Client: [redacted] **Date of Birth:** [redacted] **Date of Plan:** 26/09/2019

The neurofeedback training plan will begin with Infra-Low Frequency training to identify the optimal 'reward' frequency. Once this has been established and the response is stable, additional placements will be added as identified below. Synchrony training and Alpha-Theta training will be added as indicated below once progress has been made with Infra-Low Frquency training. This Plan will be guided and if necessary modified by the cient's response to the training.

Infra-Low Frequency Training						Alpha-Theta (AFz+Pz)	Synchrony
Left-Right (T3-T4)	Right Back (T4-P4)	Right Front (T4-Fp2)	Left Front (T3-Fp1)	Left Back (T3-P3)	Broca's area (F3-F7)		
							
Stabilisation	*Physical calming, body and spatial awareness*	*Emotional expression and reactivity*	*Mental calming, impluse control, planning, organisation, verbal & written expression, logical thinking*	*Awareness & processing detail, sensory processing, dominant hand awareness*	*Word finding and verbal articulation*	*Resolution of learned fears and habits*	*Building resilience*

Client's symptoms are mapped against these electrode placements: (= priority symptom identified for training focus and tracking)**

Sugar craving and reactivity	Poor social or emotional reciprocity (response)	Self-injurious behaviour	Unmotivated **	Reading difficulty	Poor word finding	Low self-esteem	Low self-esteem
Sleep walking	Poor drawing ability	Rages	Slow thinking	Poor attention to detail	Poor vocabulary	Fears	
Mood swings	Poor body awareness	PMS symptoms - reactive or aggressive symptoms	Poor vocabulary	Messy handwriting			
Disregulated sleep cycle	Physically Restless sleep	Oppositional or defiant behaviour	Poor verbal expression	Difficulty following directions			
	Nightmares (scary dreams often recalled) or vivid dreams	Lacking common sense	Poor sustained attention				
	Lack of appetite awareness	Lack of empathy	Poor Speech articulation - verbal expression				
	Difficulty falling asleep (physically restless)	Lack of emotional awareness	Poor short-term memory				
		Fears	Poor concentration				
		Diffiuclty falling asleep (fears & hypervigilance)	PMS symptoms - sadness, mental fog, worry				
		Attachment problems	Lack of alertness				
		Anger **	Impulsivity				
		Aggressive behaviour **	Distractibility				
			Difficulty thinking clearly				
			Difficulty shifting attention				

Example Neurofeedback Plan

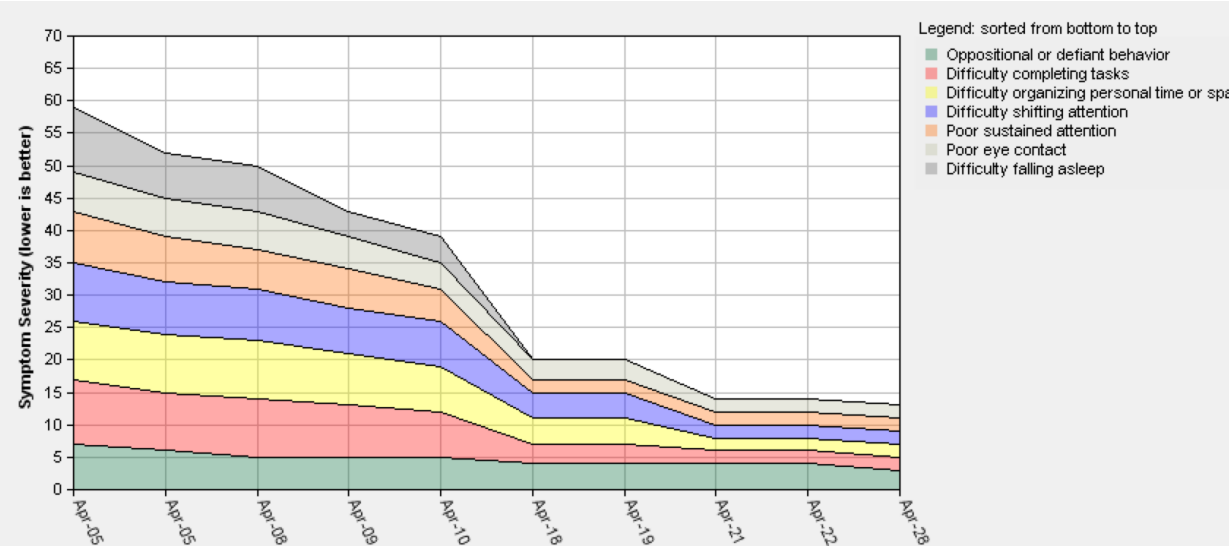
Priority symptoms (identified in the plan above with **) are rated 1-10 for severity to establish a baseline.

Neurofeedback Plans can be likened to route maps. They establish a potential route and a starting point, but the actual route taken will be adjusted according to what is encountered on the journey. In the case of neurofeedback feedback on the client's response is critical to guiding this route.

Neurofeedback therapy sessions are planned to be delivered from one of our existing clinics, or at a clinic to be set up in a more local setting, at a rate of 2 sessions per week per young person.

Measures

Measures are primarily symptom ratings together with verbal reports of progress from parents/carers. The symptoms selected for tracking are entered into an online symptom-tracking system and baselined. An email is automatically sent to clients/parents/carers twice a week with a link to click on, re-rate the symptoms and make any comments.



Example Symptom Tracking System graphical output

Financial Analysis – Return on Investment & Health Economic Analysis

Return on Investment

This analysis is based on several existing sources, together with some working assumptions*.

Basis of Estimate:

8.3% of population experiencing 4+ ACEs[45]
£287 late intervention cost average per person in UK per annum[46]
£3,458 late intervention cost per person per annum suffering 4+ ACEs (£287/8.3%)

81 year average lifespan UK
-12 average lifespan reduction assumed for 4+ ACE sufferers[45]
69 years lifespan assumed for 4+ ACE sufferers
14 age at which 4+ ACEs suffered*
55 number of life years with 4+ ACE sufferers

£191,000 lifetime cost of late intervention of 4+ ACE sufferers (55 x £3,458)
£85,000 Net Present Value of cost of late intervention (Discount Factor 3.5% pa)

We have assessed cost and effectiveness in 2 ways: A simple model based upon our private client experience where non-attendance is a negligible factor; and Decision-tree based models that allow a more nuanced analysis. We begin with the simple model.

Cost of Advanced QEEG Brain Mapping and 40 sessions of neurofeedback therapy: £3,840
Success rate at complete remediation: 80%*
Cost per successful intervention: £4,800.

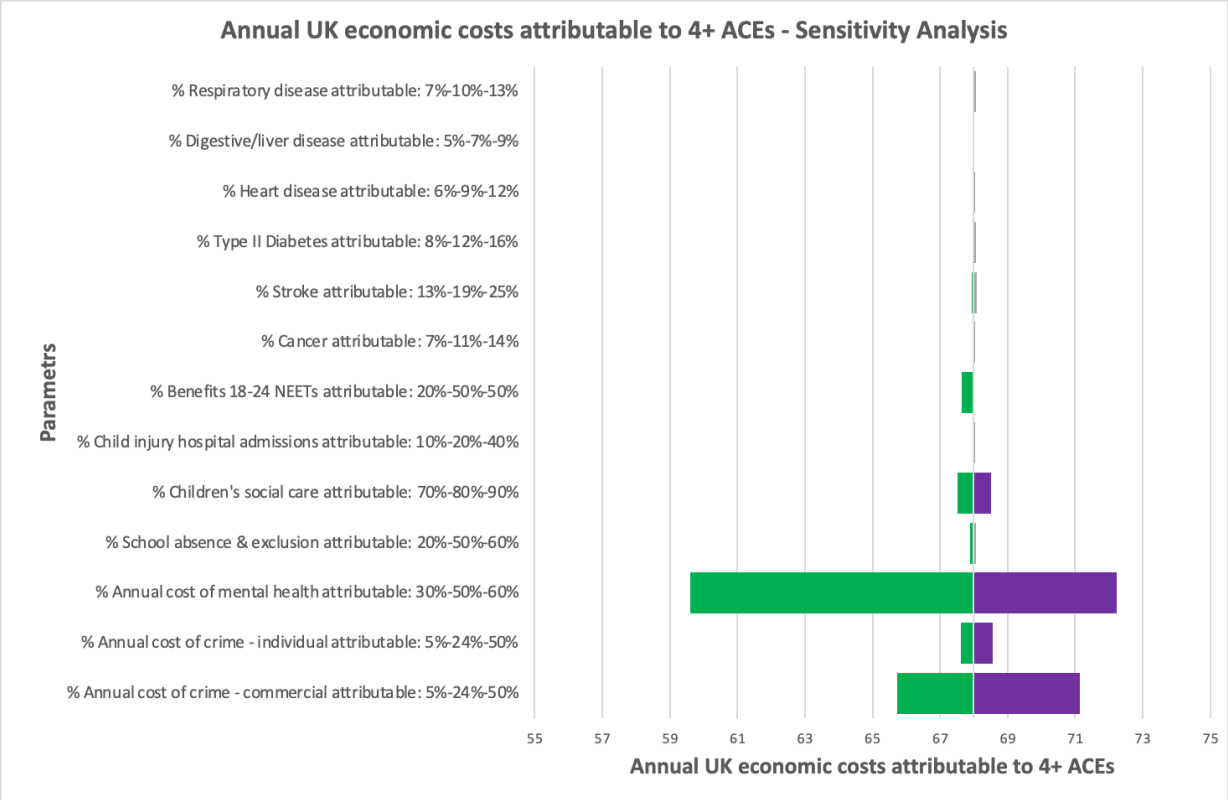
Return on Investment: £85,000 - £4,800 = £80,000 per client/patient, £80m per 1000.

This analysis is simple, but is believed to be conservative.

We have separately quantified the cost of unmitigated 4+ ACEs at £68bn per annum from a 'drains-up' analysis of the costs of crime, NEETS, children's care, mental health and chronic disease.

With 5.4m of the population suffering 4+ ACEs, this equates to an unmitigated 4+ ACEs cost of £12,500 per person per annum. This suggests the RoI above may be understated by > 3 times.

The sensitivity analysis for the figure of £68bn is overleaf. It can be seen that the estimate is most sensitive to mental health costs. The baseline figure assumes that 50% of mental health costs can be attributed to 4+ ACEs. The sensitivity analysis demonstrates that if this figure was reduced to 30% the total figure will still be > £59bn pa.



Health Economic Analysis

When the NICE Guidelines for Adult PTSD were reviewed in 2018[47], no economic analysis was performed for Neurofeedback Therapy.

We have performed an economic analysis using a simplified version of the NICE methodology, to enable comparison with other interventions. We have been grateful for the guidance of Dr Mathew Taylor, Director of the York Health Economics Consortium in this work.

NICE health economic analyses are based upon comparing changes in Quality Adjusted Life Years (QALYs) with costs.

Quality Adjusted Life Years
QALYs are based upon Utility Scores linked to Health States. A fully healthy life equates to 1 QALY per year. Death is 0.

NICE's assessment of the evidence of health-state utility data for PTSD included 3 studies.

For the QALY analysis, NICE chose an Australia and New Zealand study[48] that compared the health states of those had a 12-month diagnosis of PTSD but without a current (30- day) diagnosis, who had received CBT, with those with a 12-month diagnosis of PTSD who had not been receiving treatment. These health utilities reflect the effectiveness of CBT, and those

without a PTSD diagnosis still had a relatively low utility score of 0.635, those with a PTSD diagnosis have a health state utility score of 0.555.

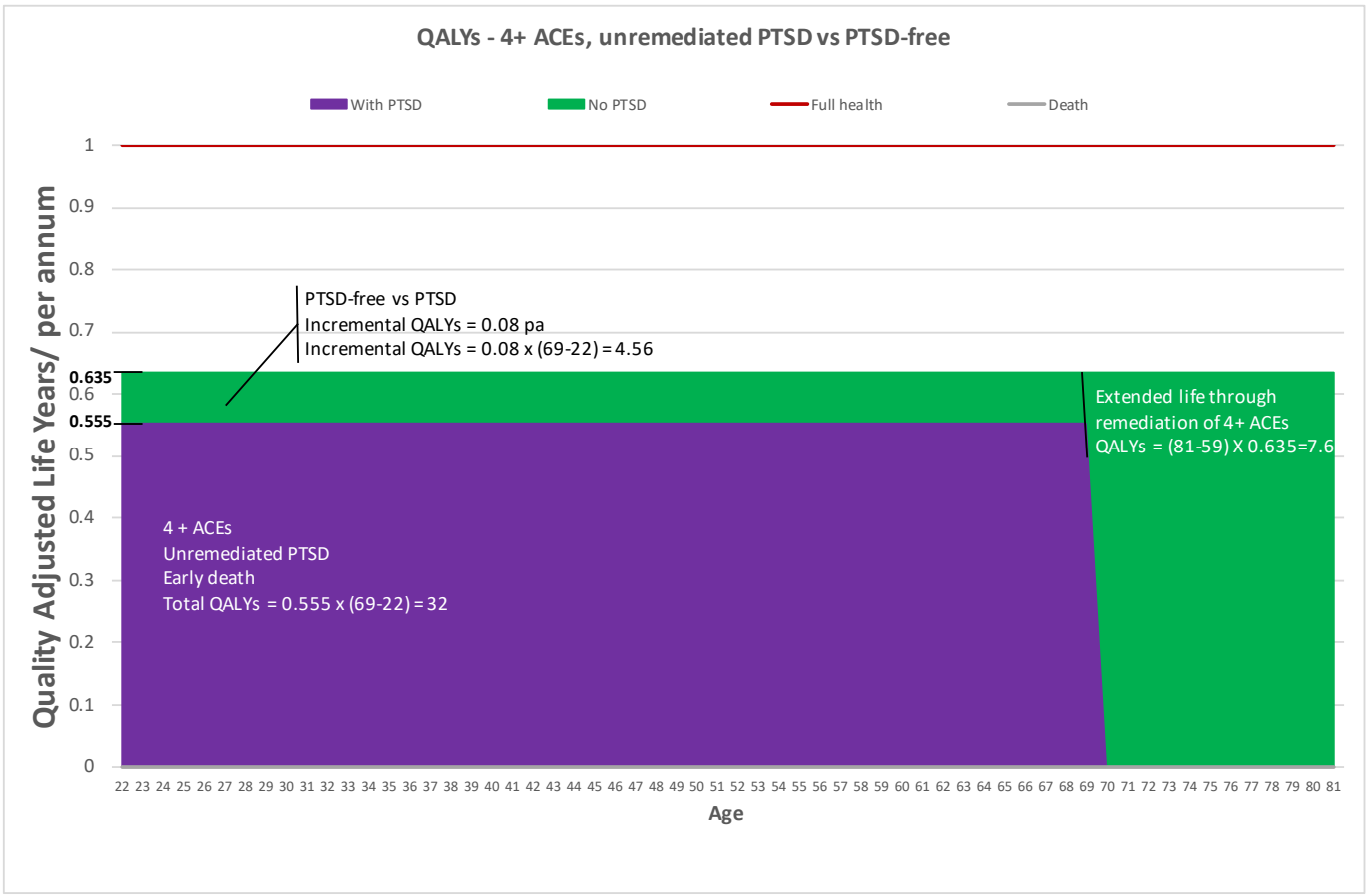
NICE decided not to use the utility scores from another study that showed a non-PTSD health utility of 0.87[49], on the basis that these reflected people who may not have suffered PTSD, and "utility values in people who have never had PTSD are expected to be higher than those in people who have remitted from PTSD[50]."

Whilst this is logical, our proposition is that early intervention will avoid the long-term health deterioration as a result of the allostatic load of the chronic stress of PTSD, and so such a health utility is very possible upon remission from PTSD. A health utility of 0.87 would be a QALY increment 300% greater than that assumed: (0.87 – 0.555)/(0.635 – 0.555) = 0.315/0.08 = 3.94.

For the sake of our analysis, we have assumed 50:50 male:female ratio, giving mean Utility Scores of 0.635 without PTSD and 0.555 with PTSD, i.e. a difference of 0.08 Quality Adjusted Life Years (QALYs) for every year of life.

Assuming that the intervention occurs at the age of 22, we can calculate the impact that successful neurofeedback therapy has on QALYs:

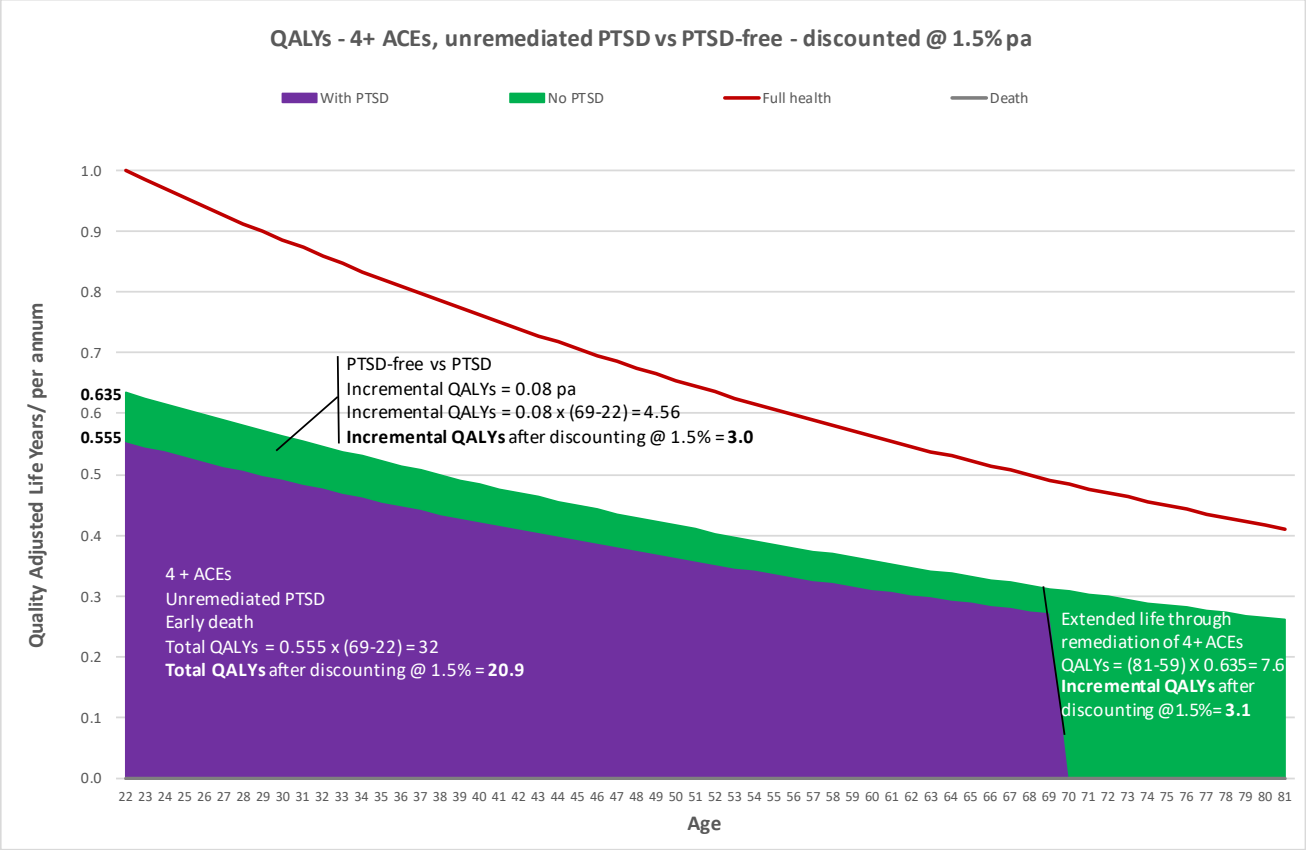
	Years	**QALYs**
No intervention – with PTSD	69-22 = 57	57 x 0.555 = **32**
Remediation of PTSD through Neurofeedback	69-22 = 57	57 x 0.635 = 36
Incremental QALYs	57	57 x 0.08 = **4.6**
Extended life through remediation of 4+ ACEs	81-69 = 12	12 x 0.635 = **7.6**



NICE recommend that QALYs in future years are discounted. 3.5% is the standard for costs and benefits (QALYs). A discount rate of 1.5% can be used for benefits lasting > 30 years[51]. The following table and graph show the impact of discounting at 1.5% pa:

	Years	QALYs	Discounted QALYs
No intervention – with PTSD	69-22 = 57	57 x 0.555 = **32**	38 x 0.555 = **20.9**
Remediation of PTSD through Neurofeedback	69-22 = 57	57 x 0.635 = 36	38 x 0.635 = 23.9
Incremental QALYs	57	57 x 0.08 = **4.6**	**3.0**
Extended life through remediation of 4+ ACEs	81-69 = 12	12 x 0.635 = **7.6**	4.8 x 0.635 = **3.1**

Additional QALYs as result of remediation of PTSD	**3.0**
Additional QALYs as result of extended life	**3.1**
Total additional QALYs including extended life	**6.1**



Incremental Costs

Incremental Costs are the differences in the costs of interventions, known as ΔC.

One comparison point is the cost of "No treatment". NICE calculate[52] that adults with PTSD cost the NHS an average of c. £1,000 per annum more than those who don't.

Over our period of analysis, for those with unremediated PTSD as a result of 4+ ACEs (55 years), this equates to £55,000, which after discounting at 3.5% pa is equivalent to £24,500 current cost.

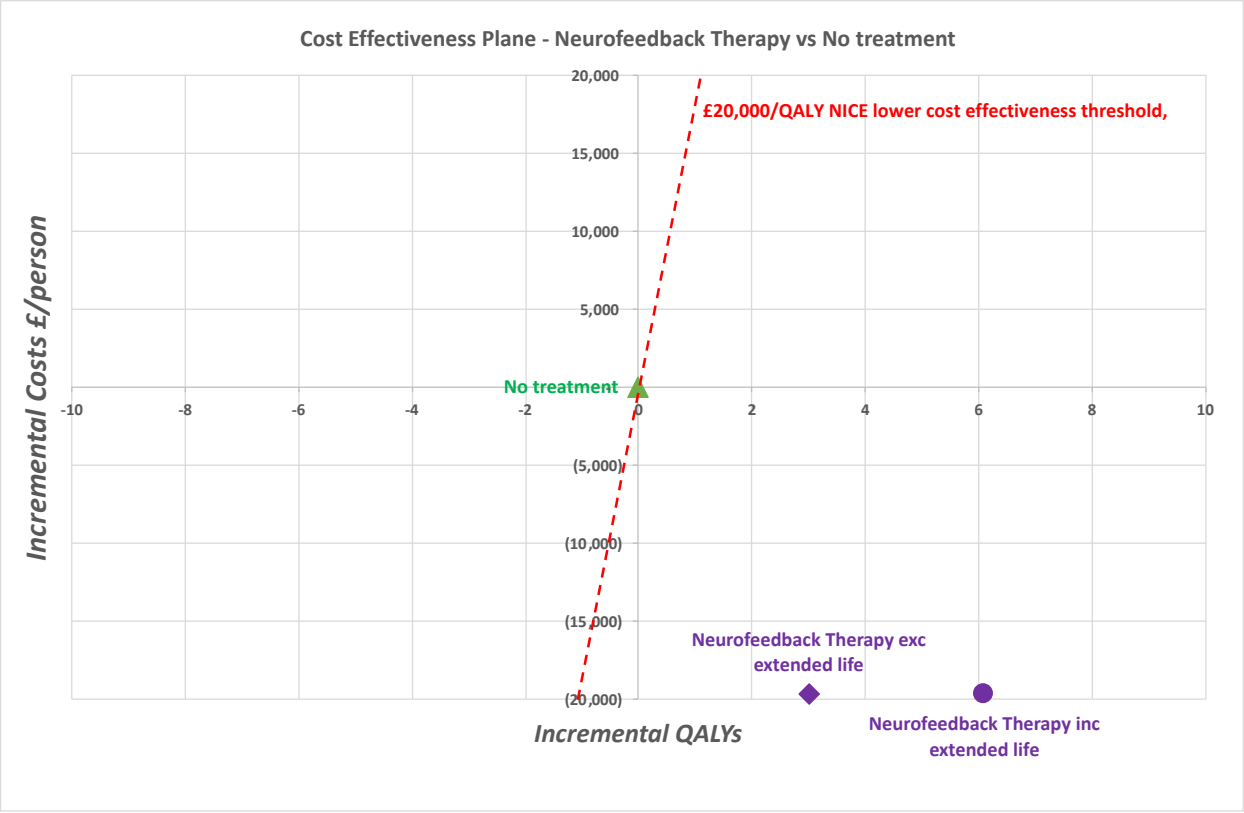
=> ΔC = £4,800 - £24,500 = - £19,700, i.e. the intervention costs less than no treatment.

Cost Effectiveness Plane

A Cost Effectiveness Plane plots comparative (incremental) costs and QALYs for a candidate intervention relative to a reference intervention. Those interventions that cost less and add QALYs should be accepted. Interventions that cost more but add QALYs will be accepted subject to the willingness-to-pay (WTP) per unit of effectiveness, set at the NICE lower cost effectiveness threshold of £20,000/QALY.

In the example below, Candidate Intervention A would be accepted, Candidate Intervention B would be rejected:

Plotting the analysis of Neurofeedback therapy vs. No treatment on the cost effectiveness plane shows that Neurofeedback costs less and adds QALYs, and on that basis would be accepted:



Comparison with other interventions

Cost Effectiveness Planes often express the data per 1000 patients, i.e. both incremental costs and incremental QALYs are multiplied by 1000.

The graph below adopts this convention, and also shows how the interventions assessed by NICE would be displayed on this scale:

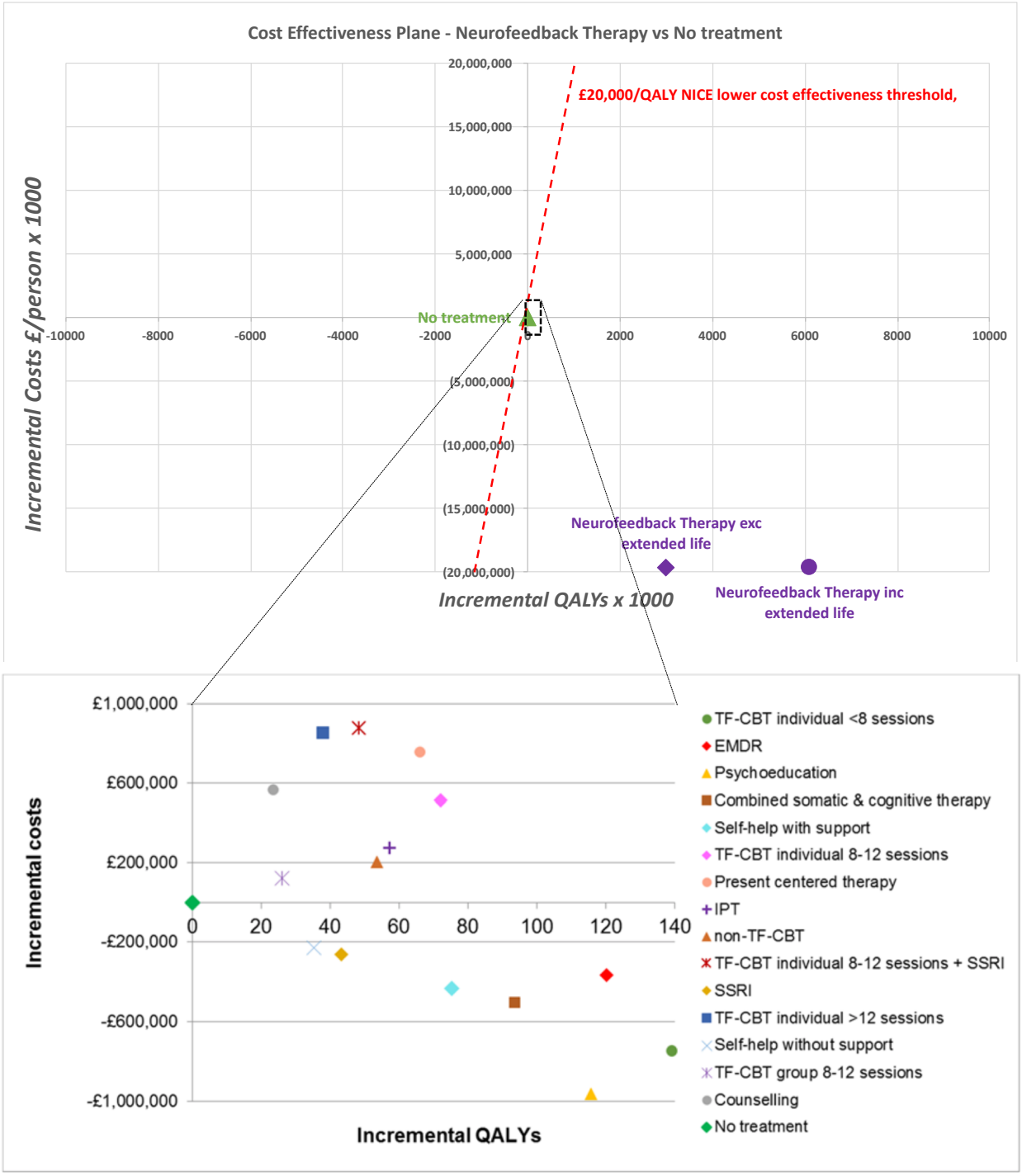


Figure 701 from Ref 52

The obvious question is why is there such a disparity between the NICE analysis and our analysis? Following discussion with an expert in Health Economics[53] it became apparent that NICE's analysis restricted the benefits to 3 years.

The rationale for limiting the analysis to 3 years is unknown, is inconsistent with academic evidence and clinical experience, and raises questions of credibility and validity.

It has a major effect on the health economic analysis, severely limiting the incremental QALYs possible within 3 years, and impacting the Net Monetary Benefit.

Net Monetary Benefit (NMB) = **E x λ – C** where E is effectiveness (number of QALYs), C are costs, and λ is the level of the willingness-to-pay (WTP) per unit of effectiveness, set at the NICE lower cost effectiveness threshold of £20,000/QALY.

For Neurofeedback therapy, NMB = 6.1 x £20,000 - £4,800 = £117,000/person.
If extended life is excluded, **NMB = 3.0 x £20,000 - £4,800 = £55,000/person.**

If this analysis is artificially constrained to 3 years worth of benefits, then there is no QALY benefit from life extension, and **NMB** = 1.84* x £20,000 - £4,800 = **£32,000/person.**

*QALYs = [QALYs with PTSD + (QALYs without PTSD – QALYs with PTSD) x % remediation] x 3yrs inc. discount factor
= [0.555 + (0.635-0.555) x % remediation] x (1 + (1-3.5%) + (1-3.5%)^2)
= [0.555 + 0.08 x % remediation] x 2.8962 = [0.555 + 0.08] x 2.8962 = 1.839

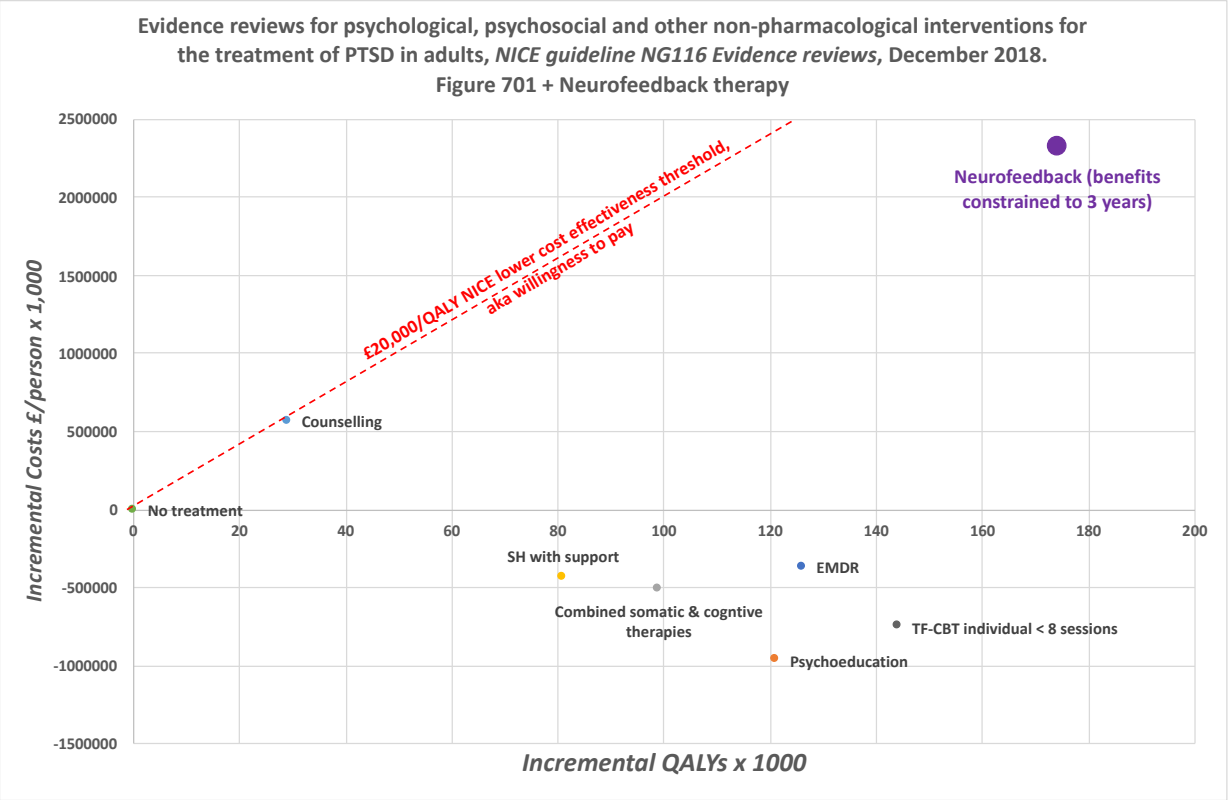
Despite this constraint, Neurofeedback therapy compares favourably with other interventions assessed by NICE. Table 204 from Ref 52 lists the assessed interventions in order of calculated NMB. We have inserted the data for Neurofeedback under this constraint:

Intervention	Mean per person			NMB £/ person
	QALY	Inter cost £	Total cost £	
TF-CBT individual <8 sessions	1.809	541	1,722	34,467
EMDR	1.791	747	2,103	33,709
Psychoeducation	1.786	109	1,506	34,214
Combined somatic & cognitive therapies	1.764	358	1,964	33,314
SH with support	1.746	266	2,036	32,876
Neurofeedback therapy	1.84		4,800	32,000
TF-CBT individual 8-12 sessions	1.742	1,181	2,983	31,865
Present-centred therapy	1.736	1,373	3,228	31,498
IPT	1.728	810	2,747	31,805
non-TF-CBT	1.724	706	2,676	31,800
TF-CBT individual 8-12 sessions + SSRI	1.719	1,326	3,348	31,022
SSRI	1.714	145	2,209	32,065
TF-CBT individual >12 sessions	1.708	1,205	3,325	30,841
SH without support	1.706	98	2,241	31,873
TF-CBT group 8-12 sessions	1.696	362	2,592	31,334
Counselling	1.694	785	3,038	30,838
No treatment	1.670	0	2,471	30,935

Extract of Table 204 from Ref 52 with 3-year constrained data on Neurofeedback inserted

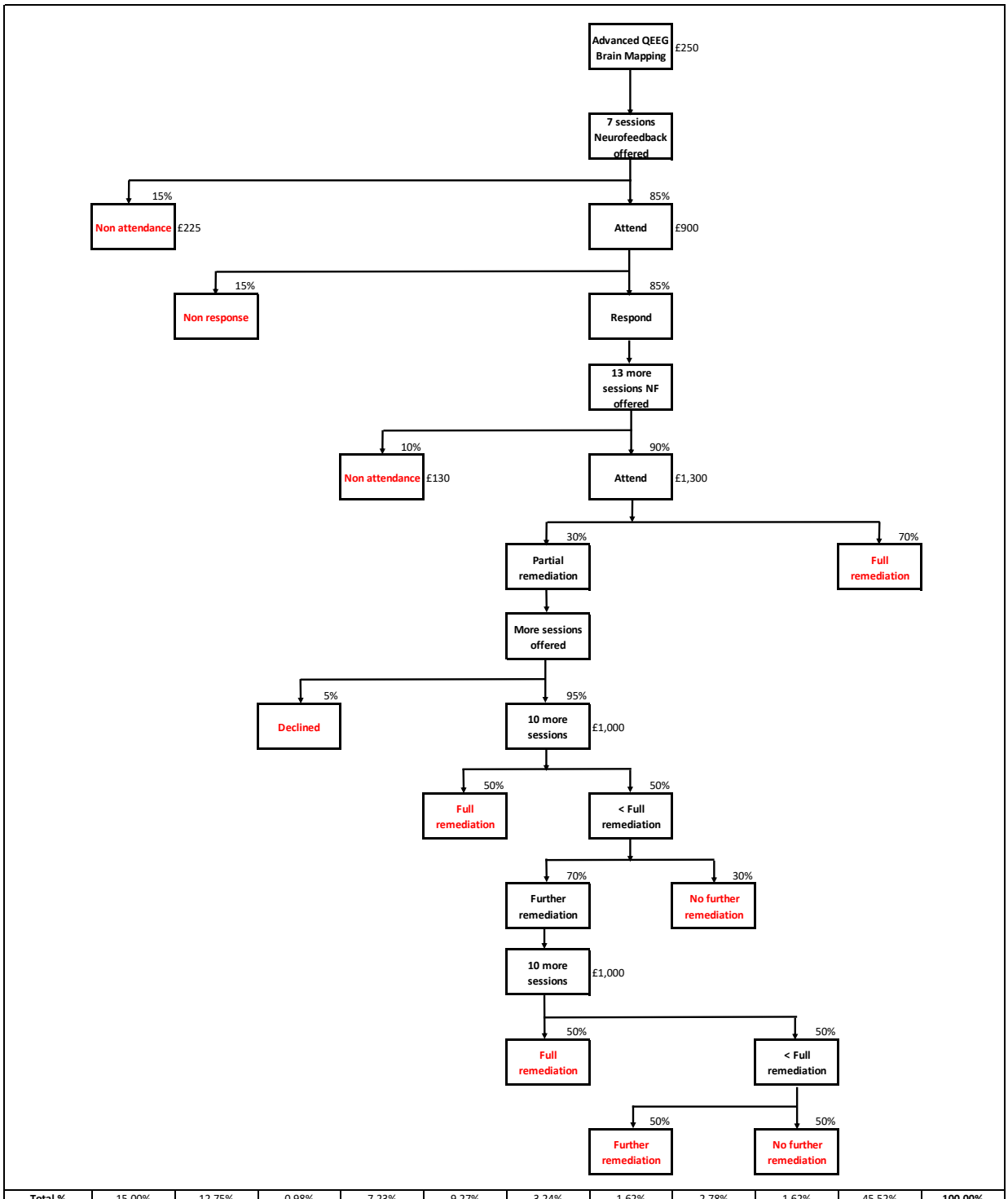
This comparison on the cost effectiveness plane relative to No treatment illustrates that Neurofeedback therapy compares favourably with NICE-approved interventions.

Whilst the incremental cost is greater than No treatment, it is clearly on the right side of the willingness-to-pay (WTP) threshold:



Introduction of Decision Tree Model

Decision trees enable a more nuanced assessment of the pathway and modelling of variability and uncertainty. The decision tree we have developed for Neurofeedback therapy is shown below. It introduces possibilities of non-attendance, and also models a staged approach to adding sessions, up to a maximum of 40 sessions, rather than the simple model which assumes that everyone will receive 40 sessions.



Total %	15.00%	12.75%	0.98%	7.23%	9.27%	3.24%	1.62%	2.78%	1.62%	45.52%	**100.00%**
Total Cost	£475	£1,150	£2,450	£1,280	£3,450	£4,450	£4,450	£3,450	£4,450	£2,450	
Remediation	0	0	0	0	100%	100%	75%	50%	60%	100%	
% x Cost	£71	£147	£24	£92	£320	£144	£72	£96	£72	£1,115	**£2,154**
% x Remediation	0.0%	0.0%	0.0%	0.0%	9.3%	3.2%	1.2%	1.4%	1.0%	45.5%	**62%**

A deterministic analysis assigns a fixed probability estimate at each decision stage. The results are shown in the bottom rows, and correspond to each of the end-stages in red above.

With the inclusion of the risk of non-attendance, the average (mean) remediation is adjusted to 62%, and with the staged approach to session management, the average mean cost is adjusted to £2,154.

The revised QALYs are calculated:

Incremental QALYs = (Full remediation QALYs – No treatment QALYs) x % remediation
= (1.84 – 1.67) x 62%
= 0.17 x 62%
= 0.105

Total QALYs = 1.67 (No treatment) + 0.105 = 1.775

We can insert these figures into Table 204 of Ref 52 to show that the NMB improves:

Intervention	Mean per person			NMB £/ person
	QALY	Inter cost £	Total cost £	
TF-CBT individual <8 sessions	1.809	541	1,722	34,467
EMDR	1.791	747	2,103	33,709
Psychoeducation	1.786	109	1,506	34,214
Neurofeedback therapy	1.775		2,154	33,364
Combined somatic & cognitive therapies	1.764	358	1,964	33,314
SH with support	1.746	266	2,036	32,876
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SH without support	1.706	98	2,241	31,873
TF-CBT group 8-12 sessions	1.696	362	2,592	31,334
Counselling	1.694	785	3,038	30,838
No treatment	1.670	0	2,471	30,935

Extract of Table 204 from Ref 52 with 3-year constrained data on Neurofeedback inserted

Probabilistic analysis

We have also performed a probabilistic analysis using a Monte-Carlo simulation. A probabilistic analysis assigns a probability distribution to each input variable.

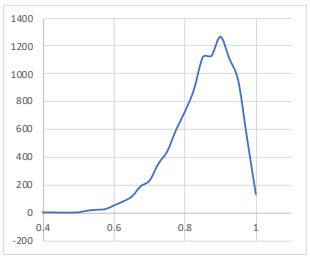
Each probability decision stage within the Decision Tree was modelled by a Beta distribution, as recommended by the literature[54]. The parameters for the Beta distribution, $\propto$ and β, were calculated using the deterministic model parameter as the mean (m), with the Standard Deviation (s) set at 10% of the mean:

$$\propto = \frac{m^2(1-m)}{s^2} - 1 \quad \beta = \frac{m(1-m)^2}{s^2}$$

For example, in the Decision Tree's first decision point, after 7 sessions of Neurofeedback offered, the probability of the outcome "Attend" with a deterministic parameter of 85%, was modelled using a Beta distribution using the parameters:

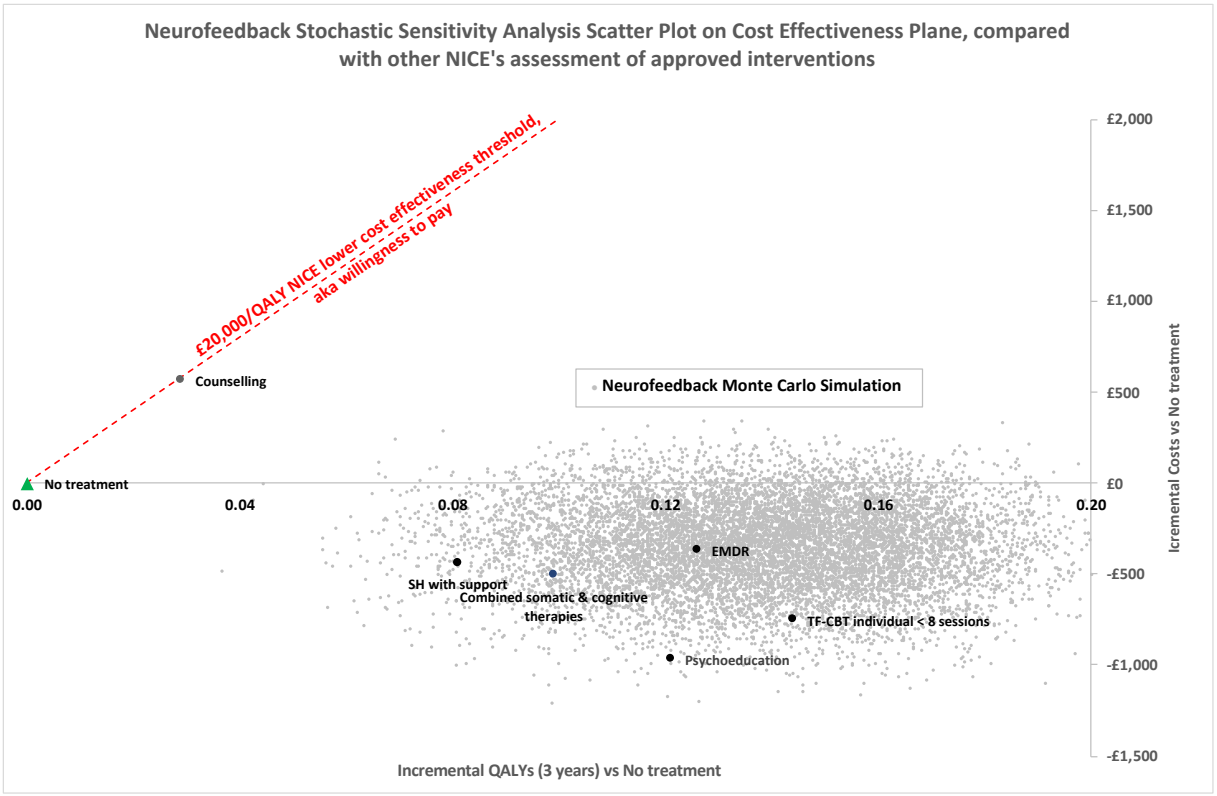
m = 0.85, s = 0.85 x 10% = 0.085
$\propto = 0.85^2.(1\text{-}0.85)/0.085^2 - 1 = 14$, β = 0.85.(1-0.85)^2/0.085^2 = 2.65

The resultant distribution for this decision over 10,000 iterations is shown below:



This is repeated for all the decision points. A simulation is then run many times, in this case 10,000 times, and the resultant multiple outputs provide a probability distribution of outcomes.

The resultant scatter-plot diagram shows 10,000 iterations on the cost-effectiveness plane, illustrating that the probabilistic analysis indicates that willingness to pay is unchallenged by this sensitivity analysis:



We conclude that Neurofeedback therapy stands up to scrutiny on health economic grounds, and is as cost effective, or more cost effective, than existing approved interventions.

It offers the NHS significant opportunity to improve outcomes and reduce costs, particularly for those who will not engage in talking therapies or reimagine the trauma.

Appendix A – ACE Questionnaire

ADVERSE CHILDHOOD EXPERIENCES QUESTIONAIRE

While the child was growing up:

1.Did a parent or other adult in the household **often** …
Swear at them, insult them, put them down, or humiliate them?
or
Act in a way that made you afraid that you might be physically hurt?
If yes enter 1: _____

2.Did a parent or other adult in the household **often** …
Push, grab, slap, or throw something at them?
or
Ever hit them so hard that they had marks or were injured?
If yes enter 1: _____

3.Did an adult or person at least 5 years older than them **ever**…
Touch or fondle them or have them touch their body in a sexual way?
or
Try to or actually have oral, anal, or vaginal sex with them?
If yes enter 1: _____

4.Did they **often** feel that …
No one in their family loved them or thought they were important or special?
or
Their family didn't look out for each other, feel close to each other, or support each other?
If yes enter 1: _____

5.Did you **often** feel that …
They didn't have enough to eat, had to wear dirty clothes, and had no one to protect them?
or
Their parents were too drunk or high to take care of them or take them to the doctor if they needed it?
If yes enter 1: _____

6.Were their parents ever separated or divorced?
If yes enter 1: _____

7.Was your mother or stepmother:
Often pushed, grabbed, slapped, or had something thrown at her?
or
Sometimes or often kicked, bitten, hit with a fist, or hit with something hard?
or
Ever repeatedly hit over at least a few minutes or threatened with a gun or knife?
If yes enter 1: _____

8.Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?
If yes enter 1: _____

9.Was a household member depressed or mentally ill or did a household member attempt suicide?
If yes enter 1: _____

10.Did a household member go to prison?
If yes enter 1: _____

Now add up the "Yes" answers: _____

This is the ACE Score

Appendix B – Discovery of EEG Biofeedback

In 1968 Barry Sterman, who was studying localized EEG patterns in relation to specific behaviors in cats, demonstrated the use of operant conditioning to train cats to generate a distinctive brainwave rhythm over the motor cortex, the part of the brain associated with movement control, when rewarded with milk[55].

This pattern, in the frequency range 12-20Hz, was termed the 'sensorimotor rhythm' (SMR).

Months later, unrelated research[56] funded by the space race into the effects of rocket fuel (hydrazine) involved injecting rocket fuel into a number of cats and observing the results as all the cats cried, vomited, salivated, and after an hour, most of them had a seizure.

Initially Sterman could not understand why a minority of the cats had not had a seizure after 1 hour, until it was realised that these seizure-resistant cats were the only ones that had taken part in the previous study to condition the cats to generate enhanced SMR.[57] The operational conditioning of the SMR had been transferred to immunity to seizures.

This experiment was repeated and then extended to primates and later humans, including an 'double-crossover' study design[58] on epileptic patients where part of the experimental protocol was to *reverse* the direction of operant conditioning at 12-15Hz unknown (blinded) to the subjects, which *increased* the incidence of seizures.

Examining the underlying neuroscience, the 'sensorimotor rhythms' (SMR) are generated within the somatosensory nuclei of the thalamus, relayed to the somatosensory cortex (where they can be picked up via scalp electrodes) and to the nucleus reticularies thalami, which responds with a similar burst, at the same time releasing the neurotransmitter GABA, which causes the process to begin again[59,53]. This back-and-forth rhythm controls excitability and enables control over motor function.

Hydrazine interferes with the synthesis of GABA[53], effectively abolishing these EEG rhythmic patterns, increasing cortical and thalamic excitability, and making the brain vulnerable to seizure when stimulated[53].

Therefore it can be concluded that the strengthening of the SMR rhythms through conditioning either increased GABA synthesis, up-regulated GABA receptors, or facilitating another inhibitory process[60].

Appendix C – References

[1] Felitti, Vincent J. "Childhood sexual abuse, depression, and family dysfunction in adult obese patients: a case control study." *Southern medical journal* 86.7 (1993): 732-736.

[2] Felitti VJ, et al., "Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study." *American Journal of Preventative Medicine* 14.4 (1998):245-258.

[3] Bellis, Mark A., et al. "Measuring mortality and the burden of adult disease associated with adverse childhood experiences in England: a national survey." *Journal of public health* 37.3 (2014): 445-454.

[4] http://www.wales.nhs.uk/sitesplus/888/page/88524

[5] Bellis, M. A., et al. "Welsh Adverse Childhood Experiences (ACE) Study." *Adverse childhood experiences and their impact on health-harming behaviours in the Welsh adult population. NHS Wales* (2015).

[6] Retrieved from https://www.cdc.gov/violenceprevention/childabuseandneglect/acestudy/about.html 25/9/19.

[7] Children Act 1989, S31 (2)(a).

[8] American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub, 2013.

[9] https://www.nhs.uk/conditions/post-traumatic-stress-disorder-ptsd/complex/

[10] https://www.mind.org.uk/information-support/types-of-mental-health-problems/post-traumatic-stress-disorder-ptsd/complex-ptsd/#.XYyFRpNKjOQ

[11] Van der Kolk, Bessel A. "Developmental trauma disorder: toward a rational diagnosis for children with complex trauma histories." *Psychiatric annals* 35.5 (2017): 401-408.

[12] Transforming Diagnosis, Thomas Insel, National Institute for Mental Health website, 2013, retrieved from https://www.nimh.nih.gov/about/directors/thomas-insel/blog/2013/transforming-diagnosis

[13] Nuwer, Marc. "Assessment of digital EEG, quantitative EEG, and EEG brain mapping: report of the American Academy of Neurology and the American Clinical Neurophysiology Society." *Neurology* 49.1 (1997): 277-292.

[14] Rose, Todd. *The end of average: How to succeed in a world that values sameness*. Penguin UK, 2016, pp.19-22.

[15] Miller, Michael B., et al. "Extensive individual differences in brain activations associated with episodic retrieval are reliable over time." *Journal of Cognitive Neuroscience* 14.8 (2002): 1200-1214.

[16] https://nebahealth.com/products/neba-adhd-brainwave-assessment-aid/

[17] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm?ID=DEN110019

[18] Kropotov, J.D. et al. “Independent component approach to the analysis of EEG recordings at early stages of depressive disorders.” *Clinical Neurophysiology*, 121.3 (2010) pp.281-289.

[19] Kropotov, Juri D. *Functional neuromarkers for psychiatry: Applications for diagnosis and treatment*. Academic Press, 2016.

[20] Ogrim, G., Kropotov, J., Brunner, J.F., Candrian, G., Sandvik, L. and Hestad, K.A., 2014. Predicting the clinical outcome of stimulant medication in pediatric attention-deficit/hyperactivity disorder: data from quantitative electroencephalography, event-related potentials, and a go/no-go test. *Neuropsychiatric disease and treatment*, *10*, p.231.

[21] Kaiser, David A. "Basic principles of quantitative EEG." *Journal of Adult Development* 12.2-3 (2005): 99-104.

[22] Sterman, M. Barry, and David Kaiser. "Comodulation: A new QEEG analysis metric for assessment of structural and functional disorders of the central nervous system." *Journal of Neurotherapy* 4.3 (2000): 73-83.

[23] Sterman, M. B., and D. A. Kaiser. "SKIL Topometric Software." *Los Angeles, CA: Sterman-Kaiser Imaging Laboratory* (2005).

[24] Kristie Brandt, C. N. M., Perry, B. D., Stephen Seligman, D. M. H., & Tronick, E. (Eds.). (2013). *Infant and early childhood mental health: Core concepts and clinical practice*. American Psychiatric Pub, p.27.

[25] Kaiser, D. A. (2008). Functional connectivity and aging: Comodulation and coherence differences. *Journal of Neurotherapy*, *12*(2-3), p 134.

[26] Cannon, W. B. (1932). Homeostasis. *The wisdom of the body*. Norton, New York.

[27] Brown, B. (1974). *New Mind, New Body Bio-Feedback: New Directions for the Mind*. Harper & Row, 10.

[28] Van Der Kolk, B. (2015). The body keeps the score: Brain, mind, and body in the healing of trauma. Penguin Books.

[29] PracticeWise Blue Menu of Evidece Based PsychoSocial Interventions for Youth, https://www.practicewise.com/portals/0/forms/PracticeWise_Blue_Menu_of_Evidence-Based_Interventions.pdf , retrieved 20/12/16.

[30] Gruzelier, J. H. (2014). EEG-neurofeedback for optimising performance. I: a review of cognitive and affective outcome in healthy participants. *Neuroscience & Biobehavioral Reviews*, 44, 124-141.

[31] Peniston, E. G., & Kulkosky, P. J. (1989). α-θ Brainwave Training and β-Endorphin Levels in Alcoholics. *Alcoholism: Clinical and experimental research*, *13*(2), 271-279.

[32] Peniston, E. G., & Kulkosky, P. J. (1991). Alpha-theta brainwave neurofeedback for Vietnam veterans with combat-related post-traumatic stress disorder. *Medical Psychotherapy*, *4*(1), 47-60.

[33] Scott, W. C., Kaiser, D., Othmer, S., & Sideroff, S. I. (2005). Effects of an EEG biofeedback protocol on a mixed substance abusing population. *The American journal of drug and alcohol abuse*, *31*(3), 455-469.

[34] van der Kolk, Bessel A., et al. "A randomized controlled study of neurofeedback for chronic PTSD." *PloS one* 11.12 (2016): e0166752.

[35] Van der Kolk, Bessel A. *The body keeps the score: Brain, mind, and body in the healing of trauma*. Penguin Books, 2015.

[36] Panisch, Lisa S., and Audrey Hang Hai. "The effectiveness of using neurofeedback in the treatment of post-traumatic stress disorder: a systematic review." *Trauma, Violence, & Abuse* (2018): 1524838018781103.

[37] Ghaziri, Jimmy, et al. "Neurofeedback training induces changes in white and gray matter." *Clinical EEG and neuroscience* 44.4 (2013): 265-272.

[38] Ros T, Theberge J, Frewen PA, et al: Mind over chatter: Plastic up- regulation of the fMRI salience network directly after EEG neuro- feedback. *Neuroimage* 65:324-335, 2013

[39] Zhang G, Zhang H, Li X, et al: Functional alteration of the DMN by learned regulation of the PCC using real-time fMRI. *IEEE Trans Neural Syst Rehabil Eng* 21:595-606, 2013

[40] Cincotti, F., Kauhanen, L., Aloise, F., Palomäki, T., Caporusso, N., Jylänki, P., ... & Marciani, M. G. (2007). Vibrotactile feedback for brain-computer interface operation. Computational intelligence and neuroscience, 2007.

[41] Othmer, S., Othmer, S. F., Kaiser, D. A., & Putman, J. (2013, December). Endogenous neuromodulation at infralow frequencies. *Seminars in pediatric neurology* (Vol. 20, No. 4, pp. 246-257). WB Saunders.

[42] Perry, B. D. (2009). Examining child maltreatment through a neurodevelopmental lens: Clinical application of the Neurosequential Model of Therapeutics. *Journal of Loss and Trauma*, 14, 240–255.

[43] Goldway, N., Ablin, J., Lubin, O., Zamir, Y., Keynan, J.N., Or-Borichev, A., Cavazza, M., Charles, F., Intrator, N., Brill, S. and Ben-Simon, E. (2018). Volitional limbic neuromodulation has a multifaceted clinical benefit in Fibromyalgia patients. *Neuroimage*, *186*, pp.758-770.

[44] Peters, Steve. *My Hidden Chimp*. Templar Publishing, 2018

[45] Bellis, Mark A., et al. "Measuring mortality and the burden of adult disease associated with adverse childhood experiences in England: a national survey." *Journal of public health* 37.3 (2014): 445-454.

[46] Chowdry, Haroon, and Peter Fitzsimons. *The cost of late intervention: EIF analysis 2016*. London: Early Intervention Foundation, 2016.

[47] Evidence reviews for psychological, psychosocial and other non-pharmacological interventions for the treatment of PTSD in adults, *NICE guideline NG116 Evidence reviews*, December 2018.

[48] Mihalopoulos, Cathrine, et al. "Is implementation of the 2013 Australian treatment guidelines for posttraumatic stress disorder cost-effective compared to current practice? A cost-utility analysis using QALYs and DALYs." *Australian & New Zealand Journal of Psychiatry* 49.4 (2015): 360-376.

[49] Haagsma, Juanita A., et al. "Posttraumatic stress symptoms and health-related quality of life: a two year follow up study of injury treated at the emergency department." *BMC psychiatry* 12.1 (2012): 1-8.

[50] Evidence reviews for psychological, psychosocial and other non-pharmacological interventions for the treatment of PTSD in adults, *NICE guideline NG116 Evidence reviews*, December 2018, p.1113

[51] NICE (2020) The NICE methods of health technology evaluation: the case for change Appendix 1 para 14.

[52] Evidence reviews for psychological, psychosocial and other non-pharmacological interventions for the treatment of PTSD in adults, *NICE guideline NG116 Evidence reviews*, December 2018, p.1120, Table 202 Annual health and personal social service costs incurred by adults with PTSD and adults without PTSD

[53] Private email correspondence with Dr Mathew Taylor, Director York Centre for Health Economics.

[54] Edlin, Richard, et al. *Cost effectiveness modelling for health technology assessment: a practical course*. Springer, 2015.

[55] Wyrwicka, W, & Sterman, M. B. (1968). Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiology and Behavior*, 3, 703-707.

[56] Sterman, M. B., LoPresti, R. W., & Fairchild, M. D. (1969). Electroencephalographic and behavioral studies of monomethylhydrazine toxicity in the cat. CALIFORNIA UNIV LOS ANGELES BRAIN RESEARCH INST.

[57] Sterman, M. B. (2000). Basic concepts and clinical findings in the treatment of seizure disorders with EEG operant conditioning. *Clinical EEG and Neuroscience*, 31(1), 45-55.

[58] Hagemann, D., Hewig, J., Seifert, J., Naumann, E., & Bartussek, D. (2005). The latent state trait structure of resting EEG asymmetry: Replication and extension. Psychophysiology, 42(6), 740-752.

[59] Wood, J. D., & Peesker, S. J. (1974). Development of an expression which relates the excitable state of the brain to the level of GAD activity and GABA content, with particular reference to the action of hydrazine and its derivatives. *Journal of neurochemistry*, 23(4), 703-712.

[60] Sterman, M. B. (1996). Physiological origins and functional correlates of EEG rhythmic activities: implications for self-regulation. *Biofeedback and self-regulation*, 21(1), 3-33.