

# Brain SPECT as Imaging Biomarker for Evaluating Effects of Novel Treatments in Psychiatry

Dan G. Pavel MD<sup>1</sup>; Steve Best MD<sup>2</sup>

<sup>1</sup>PathFinder Brain SPECT Imaging at The Neuroscience Center, Deerfield IL, 60015, USA danpavel@pathfinder.md

<sup>2</sup>The Neuroscience Center, Deerfield, IL, 60015, USA srbest@neuroscience.md

## Introduction

Complex Neuropsychiatric conditions with multiple comorbidities can benefit from new treatment approaches in addition to their medication. Among these are:

- 1 Concurrent application of **TMS** (Transcranial Magnetic Stimulation) and ketamine infusion (also known as **Combination therapy TMS + ketamine**)
- 2 **HBOT** (Hyperbaric Oxygen Therapy)
- 3 **PSE** (perispinal etanercept injection)

In our clinic, complex patients undergo a baseline Brain SPECT and occasionally a follow-up scan after treatment. We are presenting the findings for patients who underwent such repeat scans.

## Material & Methods

**Patient population:** Six patients presented with disabling Neuropsychiatric conditions of various causes after having been treated unsuccessfully for long periods of time elsewhere. The comorbidities differed in each case.

#1 62 y.o.f: on verge of suicide with Treatment Resistant Depression, grief and effects of prolonged polypharmacy.

#2 34 y.o.f: regulatory disorder of childhood, 2 concussions, post-traumatic epilepsy, RSD and major incapacitation.

#3 54 y.o.m: childhood Tourette's, ER nurse, long history of alcohol abuse, severe depression, fatigue, sleep apnea.

#4 55 y.o.f: major depression, panic/agoraphobia, chronic pain, frequent headaches.

#5 43 y.o.m: bipolar II, anxiety, impulsive behavior, family stressors, inability to hold job.

#6 77 y.o.m: 4 years post-onset of dementia induced by General Anesthesia with major cognitive, physical and emotional impairments.

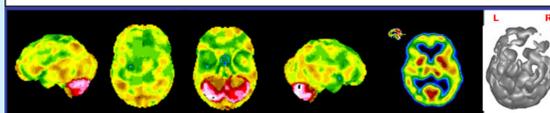
**Brain SPECT:** triple head camera with ultra-high resolution fan beam collimator. 99m<sub>Tc</sub> HMPAO.

Special software combining a set of multiparametric displays. A discrete color scale was used for the 4 sections (3 orthogonal + temporal lobe axis) as well as for a set of normalized surface display. In addition a volumetric rendition at 4 standardized threshold levels. The clarity, complementarity and user friendliness of the displays enabled reliable visual evaluation before and after treatment.

## Case #1

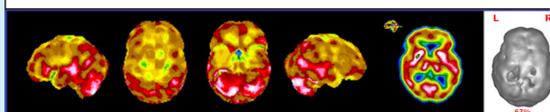
A 62 year old female on the verge of suicide. She had worked as a nurse before and following episodes of ETOH abuse, history of multiple medication administration, physical pain and prolonged family stressors (sickness and eventual death of husband), intense grief, she was

classified as treatment non-responsive following multiple treatment failures. Her formal diagnoses were TRD (Treatment Resistant Depression) and the effects of polypharmacy, which were intended to address her suffering.



**Baseline Brain SPECT**

Appearance indicates marked and extensive areas of under-perfusion in all lobes.



**Follow-up Brain SPECT**

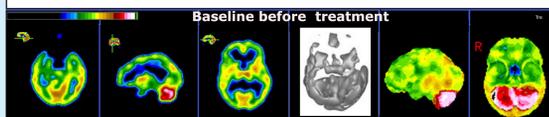
Just 5 months after treatment with combination TMS / ketamine infusion (total of 30 treatments) one can see a markedly improved perfusion across the board in cortical and subcortical structures.

This corresponded with a dramatic clinical improvement leading to major changes in her daily life: enthusiastic, rational, planning for future, taking charge of her financial and family situation and a renewed religious sentiment.

## Case #2

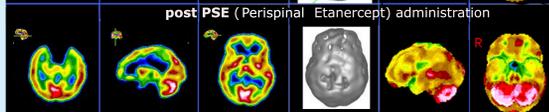
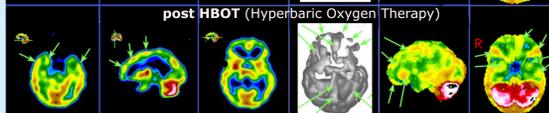
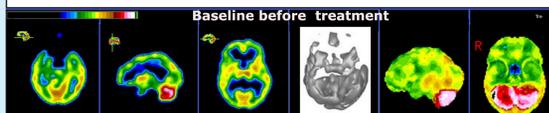
34 y.o. female presented with lifelong symptoms of regulatory disorder of childhood, two concussions, post-head injury epilepsy, and reflex sympathetic dystrophy. These ultimately led to marked suffering and extreme disability in activities of daily living. Before coming to our

clinic her medication history included over 30 types and, for almost 2 years, she spent her days in a basement with dark glasses and protective hearing gear due to intense photophobia and misophonia.



**Baseline Brain SPECT**

Images demonstrate marked and very extensive areas of under-functioning in all lobes.



**2 Follow-up Brain SPECTs**

The studies were obtained after successively applying all 3 novel treatments: 1. HBOT; 2. Combination TMS/ketamine infusion and 3.PSE). The results indicated a progressive & extensive improvement in perfusion which, in turn, corresponded to a dramatic change in the quality of her daily life and level of suffering. She now helps her family and church, had her driving permit reinstated and... has a boyfriend.

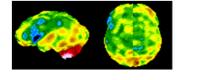
## Case #3

53 year old male with childhood-onset of Tourette's Syndrome presented with a long history of alcohol abuse, severe depression, fatigue and sleep apnea.

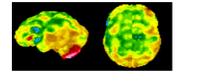
First treated with **combination TMS/ketamine infusion** and became noticeably better at the time of the 5 month follow-up SPECT. Nonetheless, he was still unable to change his lifestyle completely. At this point he finally accepted **CPAP for his sleep apnea**.

14 months later, at time of the third scan, he had resumed working (part-time job) and now leads a very different life style with a stable marriage.

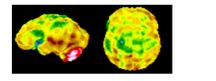
**Baseline Brain SPECT**



**5 months after 1st treatment**



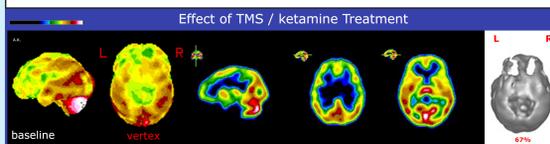
**14 months later**



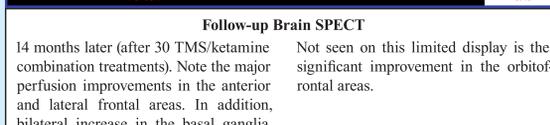
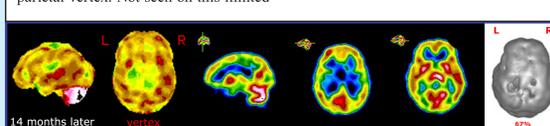
## Case #4

55-year-old female. Presented with major depression, panic disorder with agoraphobia, frequent headaches, and long-term back pain. Intermittently, she had been treated with varied pharmacologic interventions and psychotherapy for 24 years before presenting to this clinic. During that time, her symptoms did not respond to Wellbutrin, Lexapro, Abilify, Viibryd, Paxil, Nardil, Vicodin, nor conventional psychotherapy.

Combined TMS/ketamine infusion treatment was started and continued once per week for 30 weeks. Post-treatment, the patient reported markedly improved symptoms: major decrease of depression, anxiety and back pain and greatly increased levels of life satisfaction. At two year follow-up the patient had been practically free of suffering.



Note extensive bilateral hypoperfusion in dorsolateral prefrontal regions (most accentuated on the left side) and in the parietal vertex. Not seen on this limited display is the underperfusion in both orbitofrontal areas and in mesial aspect of the right temporal lobe.

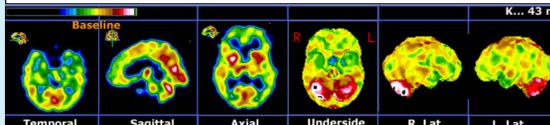


**14 months later (after 30 TMS/ketamine combination treatments).** Note the major perfusion improvements in the anterior and lateral frontal areas. In addition, bilateral increase in the basal ganglia.

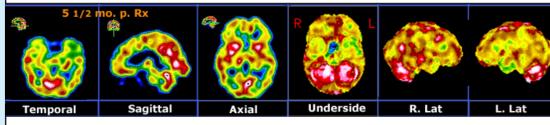
## Case #5

43-year-old Caucasian unemployed man was referred by family for TRD (Treatment Resistant Depression). Presented with lifelong symptoms of depression, anxiety, and impulsive behavior. He reported struggling with intense depressed mood, substantial life

stress, including a divorce in progress, and the inability to hold a job due to the impairment and distress associated with his symptoms. He had received psychopharmacological and psychotherapeutic treatment for the previous six years, but without improvement.



Underperfusions: in multiple hemispheric areas, more accentuated in the frontal lobes, anterior cingulate, orbitofrontal areas and apico-mesial aspect of the temporal lobes. Hyperperfusions: in the right putamen and in parts of the posterior cingulate and right cerebellum and vermis.

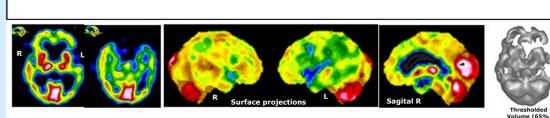


at 5 1/2 months post 24 combined TMS/ ketamine infusion treatments. Shows that practically all previously under-perfused areas have now significantly improved relative perfusion.

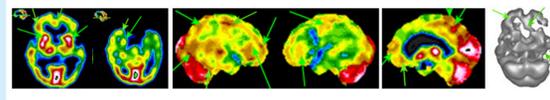
## Case #6

77-year-old Caucasian male, presented to our clinic 4 years after a knee replacement surgery. Immediately post surgery, the patient began to show dramatic cognitive, physical, and emotional impairment as compared with his pre-surgical state; these symptoms were still present when he arrived at our clinic. Diagnoses of dementia with major cognitive deficits and aphasia was established and 40-session course of hyperbaric oxygen therapy (HBOT) was initiated to address the patient's impairments.

After the first 10 HBOT treatments, the patient was also administered 25 mg perispinal etanercept (PSE) injections approximately once weekly for five months. Starting after the first PSE injection, the patient began showing progressive improvements. By the five-month follow-up, his cognitive and physical function were substantially restored. A followup 16 months after the end of treatment showed that the same level of improvements was still present.



Extensive left hemispheric under-perfusion, and multiple localized underperfusions in the right hemisphere. Involvement extends to parts of the DLPFC cortex. There is also significant under-perfusion in the temporal lobes (more on left) and to a lesser extent in the orbitofrontal areas.



At 5 months post treatment with HBOT + PSE There is overall a similar appearance but, with localized increased perfusion in multiple small areas: parts of the anterior aspect of the prefrontal cortex (including in the ventro-mesial aspect), right superior parietal, right lateral occipital, superior aspect of the left fronto-parietal area, posterior cingulate-precuneus and apico-mesial aspect of the right temporal. In addition, significant increase was seen in the striatum bilaterally.

**Observation:** while the follow-up SPECT was still abnormal, the improved perfusion in small key areas, specifically the mesial temporal lobe, prefrontal cortex, ventro-mesial frontal, posterior cingulate, precuneus and dorsal parietal, are known to contribute to memory, cognition and behavior.

## Discussion / Conclusions

The use of Brain SPECT, in this context has shown that improvements in syndrome status are correlated with changes in the perfusion pattern.

Given adequate display modalities Brain SPECT provides a useful imaging biomarker in three major ways:

**First**, it contributes to decision and tailoring of a treatment strategy, for complex cases, with multiple comorbidities.

**Second**, for confirmation/explanation of the therapeutic benefit of novel types of treatments.

**Third**, it contributes to deciding upon additional therapeutic needs or lack of thereof.

The clinical efficacy of Brain SPECT for the evaluation and treatment of patients with multiple co-morbidities and so called treatment resistant conditions, is greatly enhanced by a standardized, comprehensive display of the results. This includes a user-friendly, color, multi-parametric set of 2D and 3D images. While this type of display has withstood the test of time, a similar but more efficient software is now available in a further amplified format (see right panel). The automatic generation of a comprehensive PDF document of professional quality, minimizes operator intervention, maximizes efficiency and provides great consistency. The software is now also available remotely by uploading a reconstructed data set to a dedicated server.

**Overall this is one more example of perfusion Brain SPECT being clinically relevant in Psychiatry/ Neuropsychiatry.**

## References

1. Best SRD (2014) Rapid relief of treatment resistant depression by facilitated ketamine infusion: A preliminary report. *Activitas Nervosa Superior* 56: 28-36.
2. Best SRD (2015) Combined ketamine and transcranial magnetic stimulation for treatment resistant depression in the context of chronic OCD: A case report. *Neuropsychiatric Electrophysiology* 1:1-4.
3. Tobinick E (2014) Immediate neurological recovery following perispinal etanercept years after brain injury. *Clinical Drug Investigations* 34: 361-366.
4. Best SRD, Griffin BP, Pavel DG (2015) Ketamine and transcranial magnetic stimulation treatment for bipolar II disorder: A case report. *Journal of Medical Case Reports* 9: 1-4.
5. Steve Best, Dan G Pavel (2016) Effective Stepwise Anti-inflammatory Treatment for Markedly Disabling Neuropsychiatric Comorbidities: A Case Report. *Journal of Neurology & Neuroscience*. Vol.7 No.4:138
6. Steve Best, Dan G Pavel (2017). Combined transcranial magnetic stimulation and ketamine for treatment of refractory mood disorder, anxiety, and pain: A case report. *Curr Neurobiol* 8 (1): 1-4
7. Steve Best, Dan G Pavel (2017). Treatment of post-anesthesia dementia with perispinal etanercept injection and hyperbaric oxygen therapy: a case report. *Journal of Medical Case Reports* (2017) 11:105

## The Future: automatic, comprehensive display of results

Example of the full set of images as obtained from the newest software variant<sup>(1)</sup> we are now in the process of switching to.

The example chosen is the baseline SPECT of case #4 (see third column) and it contains 6 pages.

The first 5 pages are part of an automatically generated PDF.

Page 1: distribution of maximum cortical activity, rendered on standardized brain.

Page 2: maximum activity distribution in atlas space (without the 3D effect generated by the anatomical rendering). It provides the mid-sagittal planes as well. A set of anatomical reference sketches is also included for reader orientation.

Page 3: six standard orientations of volume rendered displays at 4 fixed thresholds.

<sup>(1)</sup> Good Lion Imaging LLC, Columbia MD, 21045. Tel: 847-987-5216; www.goodlionimaging.com

