Differential Brain Imaging For Evaluation Of Food Coloring Challenge

(Obtain enough data for a petition that inmate NE should be treated in a psychiatric hospital rather than prison.)

To: The Virginia Dept. of Corrections Human Subjects Research Review Committee (HSRRC), Dave Wiskman, chair, hsrrc@vadoc.virginia.gov

From: Dr. Edward H. Takken, PhD, ed@takken.us, July 26, 2022

Medical Objective: Demonstrate that the brain response of inmate NE to Red 40 artificial food coloring is abnormal in centers for judgment and aggression control. His crime at age 17 was chocking his girlfriend to death in an outburst of rage.

Legal Objective: The brain imaging measurements proposed here are designed to relate to the following questions. 1) Was the inmate's rage murder temporary insanity? 2) Was the Court-ordered psychiatric evaluation used in his initial trial probably irrelevant? 3) Should he be treated in a psychiatric hospital instead of a prison? 4) Is he victim or criminal? If interpretation of the data suggests that answers to these questions are affirmative, two things might follow. NE may want to petition his sentencing judge. And VADOC might consider better limiting of artificial ingredients in foods as a means for easier control of potentially difficult inmate populations.

Medical vs. Legal: The EU and China have removed artificial colorings from foods. But in the US the prevailing medical opinion is that artificial ingredients are not related to hyperactivity-class conditions, and that evidence attempting to support restricted diets is flawed by placebo. The SPECT/PET measure of response proposed here is inherently placebo free, and the objective is to convince legal authority, not the US medical community.

Protocol: Testing needs to be in two phases. First use simple subjective evaluation to see if a few drops of Red 40 have any effect at all, and then over days work up in amount until NE thinks he feels something or observers think they see change. Arrive at a conclusion for how much NE is willing to tolerate and that observers think is safe, and then use this amount as challenge in the final SPECT/PET imaging. See "IRB" and "Safety" below. (Reaction time is expected to be ≤ 5 min for initial onset and some 10-15 min for full response. A newspaper reporter once said of his kids, "Give 'em M&M's and they're taking the wallpaper off before you can get out the door.")

For the final brain imagery an important preparation is to avoid all artificial additives for several days. Then take a a pair of brain images about 30 min apart with challenge ingested immediately after the first image. Are the images different? We call this "differential imaging."

Previous Brain Imagery: The challenge protocol has not been used before, but there has been a cross-over study using EEG imagery for a group of ADHD children when on a restricted diet or not. Interpolation of Uhlig1997 implies the following for a challenge study:

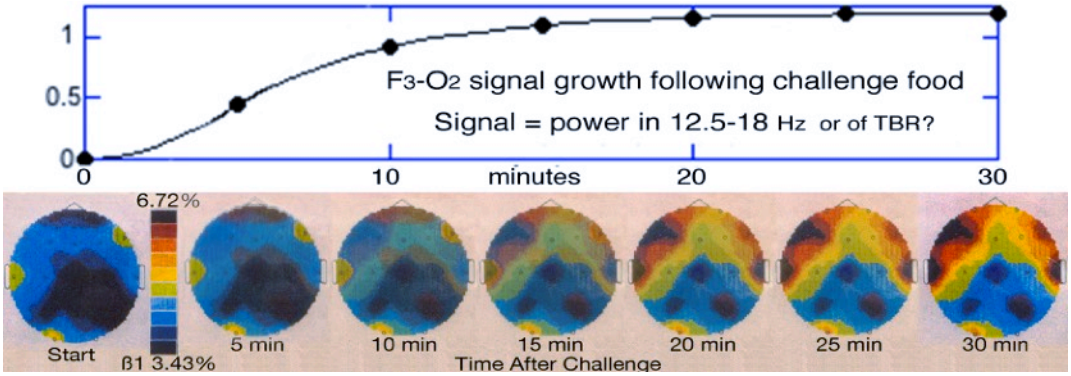


Figure 1: Anticipated EEG Response To Artificial Food Challenge For ADHD-Class Patients. The first and last images, and the first and last points of the graph, are numbers measured in Uhlig1997. The middle images are interpolation using Photoshop. F_3 and O_2 are EEG scalp electrode locations. ADHD behavior was observed to be in association with the right-hand image during uncontrolled diet.

After Uhlig1997, the next most relevant brain imagery for this proposal is a well-known Raine1998 study using metabolic PET to evaluate 38 convicted murderers. Background checks established that 12 had suffered significant abuse or depravation while 26 were from benign or supportive backgrounds. PET scans confirmed this division, but with a surprise. The 12 from abusive backgrounds had normal brain metabolism. It was the 26 from benign backgrounds that were different. They averaged 5.7 % less metabolic activity in the medial prefrontal cortex and 14.2 % less in the right orbitofrontal cortex. These are thought-judgment-conscience regions that normally control impulses from the primitive limbic system but in the benign-background criminals are apparently suppressed to the point of not being unable to do so. Raine1998 assumed this abnormal brain metabolism to be a fixed anomaly with criminality defined by innate brain state. And in general, American psychiatry has held to the position for 50 years now, that ADHD class conditions are fixed, hard-wired brain anomalies.

Walsh is another researcher who by other means found the same division of incarcerated murders into the two groups of those with significant abuse or depravation in their backgrounds but many from benign or supportive backgrounds and families thrown into distress.

Rationale For This Proposal: Raine publications including the 1998 work and later books do not reference Uhlig1997 and seem to be unaware of the variability finding reported there. EEG is less quantitive, but the cross-over study by Uhlig et al. did show that brain activity can be causally variable. The pre-frontal cortex was most affected by ingredients in foods, and the change was associated with increase in hyperactivity.

But Uhlig1997 has been referenced only twice in the medical literature—in a listing and with just a comment that placebo control was inadequate. My critique here of that critique so universally implied is that it is totally backwards boxed in thinking that misses a foundation fundamental about how to establish truth. Brain imagery should be placebo free.

Fifty years of ADHD research has been based on double-blind placebo control with observed behavior the measure of effect, and with disguise of challenge substance so limiting or incorrectly implemented as to almost assure false negative outcome. Single brain images are not considered to be adequate for diagnostics, but overlooked for decades is that *change* in brain images in response to challenge offers a measure that is both objective and diagnosstic. It is independent of whether the test subject or experimenters know what substances are being ingested or whether a challenge is being administered, and the amount of challenge substance does not have to be limited to disguise recognition.

What Challenge: The substance to be evaluated in the tests proposed here is simply the leading possibly problematic ingredient in the food/drink NE was getting in the day before his fatal outburst. That appears to be Red 40 food coloring. The amount NE was getting in his diet before his rage outburst was some 40-80 drops or maybe a teaspoon per day from Hawaiian Punch alone. That's 4-8 times the government-recommended limit, plus there was more of both Red 40 and several other additives from Fruit Loops and other snacks.

These numbers are based on NE's written response to my inquiry about what he had been eating on the day of his outburst. Also indicative is that, now that he's aware of the problem, he reports sensing reaction to food coloring. He did not describe what he can control in prison or how he reached this conclusion.

Red 40 McCormick food coloring can be purchased in any grocery store, the non-glass plastic dropper container probably preferable for this program. (Data obtained with this standard product, though, may not be of any use to the FDA . The standard FD&C colorings contain a slight bit of preservative, and by law the FDA is required to use only single compound.)

Control Volunteer: In addition to showing brain metabolic response to food coloring by NE, it would be best to also show that this does not happen in normal individuals. So the SPECT/PET equipment is being scheduled to take four head images in succession–NE, V, NE, V. I could be the volunteer, but I might not be a very good "normal." I don't feel anything from 20 drops of Red 40, but do have extensive chemical sensitivities and find perk from Coke to be stronger than from an exact same amount of caffeine. A better "normal" volunteer is needed.

Brain Imaging Techniques and Choice Of Facility: PET and SPECT should be truly objective, but both are slow using about 30 min to take one 3D image. Of the two, PET gives better and more standardized detail but may be too expensive. The image-taking rate of EEG would be ideal for capturing the brain response transition anticipated here, images taking < 5 min and in succession, but they are 2D pseudo images, and EEG is only partly objective. Personally I think it's OK the way Uhlig1997 did it with extensive data averaging, artifact screening and patient setting control. And they were able to claim consistent EEG image results when comparing 15 patients. But there seem to be no EEG facilities familiar with the data processing and controls of Uhlig1997, so I'm considering using EEG only as a secondary simultaneous measurement technique.

Request for price quotes have been sent to the PET, SPECT and EEG capable facilities near Virginia Wallens Ridge State Prison. The patient being a prison inmate was mentioned, but this needs to be reviewed more thoroughly in final negotiations.

Table 1: Medical Centers Near Wallins Ridge With Brain Imaging Capability

Medical Center	adress	distance	PET	SPECT	EEG	fMRI	SPECT+EEG
Lonesome Pine Hosp 276-523-3111	1990 Holton Ave E Big Stone Gap, VA 24219	12 mi	N	N	N	N	N
Norton Com Hosp 276-439-1000, Rad-1333	100 5th St NW Norton, VA 24273	17 mi	N	N	N	N	N
Cancer Center 276-679-5874	671 Hwy 58 E Norton, VA 24273	17 mi	PET only	N	N	N	N
Holston Valley Med Ctr 423-224-4000, EEG-5190, PET/SPECT/Rad-6815	130 W Ravine Rd Kingsport, TN 37660	52 mi	PET +CT	dual head	Y	N	?
Johnson City Med Ctr 423-431-6111, Rad-6761, EEG-6700 Doris	400 N State of Franklin Rd Junction City, TN 37604	65 mi	PET +CT	dual head	Y	?	?

Table 2: Schedule:

Test	Location	#, Duration	Objective	Start	Report
1: Preliminary Evaluation: Record is kept of when and what NE thinks he feels after ingesting Red 40 food coloring. This is done on three to five occasions for different amounts of coloring starting with a low dose.	At Wallens Ridge, maybe in cell	≈4 tests. 3-5 days in-between,	Two decisions A: Proceed or not B: Plan amount of Red 40 to be used with SPECT/PET	when proposal approved	4 weeks after start

Test	Location	#, Duration	Objective	Start	Report
2: Take two SPECT or PET images. Ingest Red 40 immediately after 1st. Wait 20-30 min before starting 2nd. A series of EEG images may be taken during the wait period. Do this both for NE and for a normal control subject.	At a medical center near Wallens Ridge	One test session. Requires a half day trip to a medical facility	Determine whether Red 40 suppresses prefrontal judgement control areas of the brain of inmate NE	Time to schedule facilitiy is about three weeks	2 mo for report to VDOC, 6 mo to included EEG

Requests For Security and Support From Wallens Ridge:

1-The main request is for NE to be transported once to a medical facility in Norton, Kingsport or Junction City. Which facility will be used is not yet determined, but for prison personnel they should be pretty much the same. Round trip travel and time at the facility is about half a day, so this probably requires something like three man-days of support for two guards plus driver.

Request is also made to consider a second trip to the same facility so as to take "calibration" imagery with caffeine used for the challenge instead of Red 40. This would probably enhance interpretability of the results, but cost at this point is unknown. The additional trip might exceed available funds, and Covid risk is a factor. Would VADOC even consider an additional trip?

2-Establish the methods to be used for guarding NE during transport to and from, and in the medical imaging facility. My expectation is that Wallens Ridge security will require NE to wear some form of restraint when in the medical facility and especially as and after he is given the challenge intended to demonstrate heightened response. The procedures security requires and the number of guards and their presence and positioning needs to be written down and sent to the medical facility, or perhaps better, sent to me for forwarding to the medical facility during our price negotiations.

3-Purchase the suggested McCormick Red 40 food coloring. The total needed is probably less than two teaspoonfuls and maybe less than one. There needs to be a place to keep it.

4-Determine a method for doing the preliminary testing inside the prison facility. Do prison personnel administer the Red 40, or since the McCormick plastic drop bottle is so small is it permissible to let NE handle it himself? The step-by-step actions needed are, 1) administer a dose of Red 40, 2) record response degree and timing over 15-30 min as noted both by an observer and by NE's description. 3) Wait a few days. 4) Repeat the procedure with a dose double the previous amount. 5) Conclude when NE's response or the observed response is significant and in discussion with me decide the amount to be used as challenge in the medical imaging facility. Part of this conclusion is judgement about safety.

5-During the preliminary testing and especially before the final SPECT/PET imaging, please allow me to see menus in advance by email or web page. And let me communicate by phone with NE to discuss items he needs to avoid and find supplement for—or discuss with kitchen personnel in person or by phone items that might be a problem and with them figure out how to modify or supplement. The most likely problems are desserts, jello, sauces and standard-purchase products with a long list of ingredients. By what means could I provide "supplement" if needed? And alternatively, would it be more feasible to have me or a FAUS volunteer daily bring in specially prepared meals?

The reason for careful diet control before testing is that even infrequent infractions can become a steady state with no or little reaction observable. There is no way that true strict control of ingredients can happen, but fortunately I've been impressed by prison food, at least at the Fairfax County Adult Detention Center. NE passed his court-ordered psychiatric

exam with rather spectacularly no symptoms found for hyperactivity or aggression. My interpretation is that the Fairfax food had far fewer offending ingredients than what he was getting at home before his crime. So the Wallens Ridge menu might OK as is, too. Also my guess is that NE is a strong enough reactor to Red 40 that tens of drops of it will still cause observable brain metabolism reaction even if he is already reacting somewhat to some other chemical he has ingested in the last few days. Still, to assure results in the SPECT/PET imaging, it would be best to eliminate as much as possible all artificial food ingredients and salicylates.

6-Please remove or raise the two-page limitation on the size of US mail that I can send to NE. I'd like to be able to send him references and documents like this one.

7-It would be good for me to visit NE inside the prison and also to ride with him both ways to and from the medical facility. Please allow it. I'd rather not drive the 860 miles round trip to Wallens Ridge to do this and instead do all the communications by email, USPS, phone and video conference. But I have to do the drive if I am to be the test reference subject, and it would be best and certainly interesting to have a good working relationship with the guy in trouble from my son's high school.

Safety: The plan as described starts preliminary testing with low Red 40 dose amount not likely to cause any effect and then increases dose amount every few days until it is decided by prison staff observation and by NE that a maximum useable dose level has been reached. Just what "maximum useable" means is discussed at length below, but the point here is that this is the dose level to be used as challenge between two SPPECT or PET images to be taken at a medical facility. And the intent of the challenge is to stimulate a high enough brain metabolic reaction to be observable in the difference between pre and post images. So before going to the imaging facility Wallens Ridge security should repeat test this maximum dose amount in house under fully prison-controlled conditions for two safety reasons—to let NE be doubly sure he knows what this dose level feels like and that he is comfortable with it, and similarly for prison security to be doubly assured the dosed inmate can retain self control.

An additional thing to do, or maybe good to start with, could be to have NE avoid caffeinated drinks for a few days and then take a significant single dose of it, such as an over-the-counter 200 mg tablet (without coloring). Does he feel any surge or observers see effect, and is it large/small or similar/different from Red 40 food coloring? This falls under safety in the sense of NE learning what to expect from everything and therefore not loosing control.

To assure safety both for the inmate and for prison personnel, note importantly that the inmate's reaction to single-dose Red 40 should not be episodic, but instead should be a peak rather like the four hour half life of caffeine. Unpredictable episodic response should occur only when a sensitive person is maintained on regular doses of artificial ingredients as in many average diets. This is what was happening to NE before his violent event. His school system had already placed him in a specialty school for problem students. Prison food undoubtedly has some additives violations but probably not a lot, so that NE's peak of response to an additional intentional large single dose of Red 40 coloring should be limited in time.

There should be no spontaneous rage, only inclination for irritation if provoked during the peak period. The provocation with his girl friend was his not being able to attend the senior prom because she had reported him as threatening preiously. When being given challenge dose of Red 40, either in the prison or in the SPECT/PET medical facility, there will be no such provocation, and he will not be alone with a physically weaker female. The presence of prison guards should dampen rather than provoke emotion. And he will be consciously choosing to test and observe himself. So probability of altercation is very low to nonexistent, even if he has taken a lot of Red 40.

The “maximum useable” dose amount of Red 40 coloring is to be established jointly by what NE senses and what prison personnel observe in response to the current dose level. At high dose levels Red 40 may make NE feel unpleasantly unsettled, thinking muddled, on edge, racy or hyper to the point that he knows he does not want to try still higher dose. Observers are not looking for hostility or rage, but instead just unsettledness or difficulty sitting still.

Medical Facility Safety: Arrangement will be made to not use the general public entrance or check-in list but rather use a delivery entrance and freight elevator. The inmate will presumably be wearing constraints with his hands behind his back while entering and walking through the facility, but this presents a problem for use of the SPECT/PET imaging machine. The patient has to be lying down on his back in the imaging machine. So guards will need to let NE’s hands be in front for about an hour and a half—about 30 min each for first image, challenge Red 40 & wait, and then the second image.

Inmate Signature: For SPECT and PET imaging the patient needs to have a small amount of radioactive tracer injected by IV. A single injection is sufficient for taking two images. There is a wait of about 20 min before imaging can start, and each image takes 30 min to complete. We plan a 20-30 min break between them. These imaging procedures are very common with quite low radiation exposure, but the patient has to sign a release form before the medical facility can proceed.

Inmate Awareness, Interest, Privacy: NE expresses interested in having these tests done. Maybe he wants to know the answer too. And from his point of view I think he probably wants to show everyone the results, not hold them private. And that probably includes all his trial records including his school records and maybe especially the results of the court-ordered psychiatric exam, which show no rage or ADHD inclination at all, but were not taken when he was under what had been his “normal” influence of artificial food ingredients.

Author Vita/Resume:

PhD in theoretical physics, Ohio State University, 1967

37 years as analyst in research and development at the Naval Research Laboratory

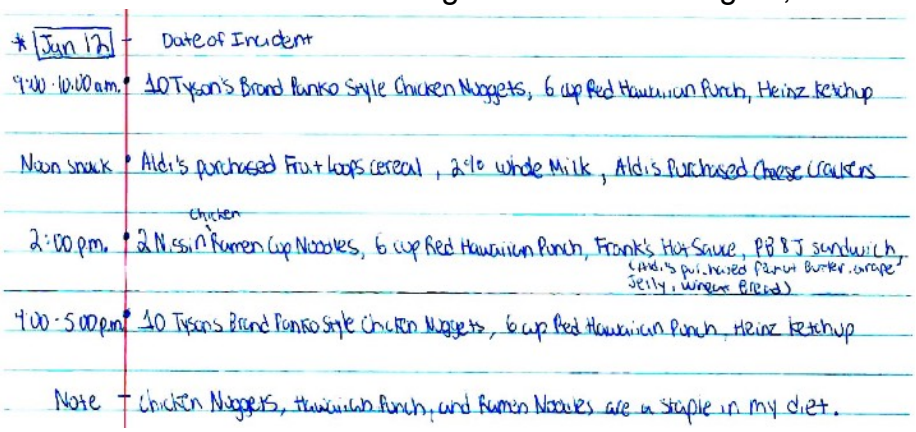
Publications ≈75 many classified, Patents 3, Clearance was TS

Currently retired with no university or IRB filiation

I am a retired research physicist with personal and family experiences that led to doubt about some aspects of medical practice and then to extensive study of select parts of medical literature. My son had many allergies and quite disruptive ADHD that pediatricians failed to recognize or treat. Then when he was ten in 1977 my wife decided to try “the Feingold diet.” The abruptness and degree of change was amazing to see. He went from a kid in trouble to an academic star beyond my conception, and she changed, too. Her mood swings disappeared, and since that was quite unexpected it could not have been placebo. So I had to wonder why official psychiatry denounces Feingold’s 1974 book on diet controls and the self-help group he started called the Feingold Association of the US, FAUS. I studied texts on brain physiology and anatomy and eventually read quit a bit of ADHD medical literature and in particular all or it in the 1970-1985 time period, and concluded that ADHD and some forms of depression and aggression are related conditions caused by disruption of enzymes in the brain. As described at ADHDBasics.info, works by Sanaiko, Ingram and others in the 1990s suggest that some chemicals when ingested can overload cleanup enzymes, typically in people who have had extensive antibiotics. Overload of PST apparently causes increase in MAO and thereby suppression of dopamine and other monoamine neurotransmitters in the brain. US psychiatry holds that the conditions are distinctly separate, caused by genetically inherited, fixed, hard wired brain anomaly that is medically uncontrollable except by opioid-class medication override.

Funding: I am the sole funder with no institutional or other financial support.

IRB, Institutional Review Board: NE was asked to help edit this proposal and has a copy of the final. He understands why and that he is to ingest Red 40 food coloring several times in preliminary testing starting with a low amount and working up to a significant amount for which he senses definitely noticeable but not too uncomfortable reaction so that brain imaging may be likely to measure something. And then for final SPECT/PET testing, he understands that this will then be the amount of food coloring he will need to ingest, that radioactive tracer will be used, and that VADOC may require him to wear some form of restraints when in the medical facility for this final testing. He has advance signed a consent form of his own making stating that he understands and agrees to all of this. He seems to want to see what these measurement show.



How I Met NE: We've never met in person and I have received correspondence from him only four times. A 2018 newspaper article about his conviction described him as "a stellar student who had been accepted to multiple colleges and played basketball, but who had anger issues" and had been sent in his senior year to a school for problem teens. This prompted me to write to him and ask about both his background and the foods he had been eating. His 11/3/19 response was thoughtfully written and gave the detail I had asked for. I concluded I can work with him but have been delayed by the Covid pandemic and by difficulty getting an IRB evaluation. Here's his list of foods just before the crime.

Foods Eaten The Day Of The Murder, Jan 12, 2018:

9-10 am	10 Tyson's brand Panko Style Chicken Nuggets, 6 cup Red Hawaiian Punch, Heinz Ketchup
Noon	Aldi's purchased Fruit Loops cereal, 2% whole milk, Aldi's purchased Cheese crackers
2 pm	2 Nissin Chicken Ramen Cup Noodles, 6 cup Red Hawaiian Punch, Frank's Hot Sauce, PB&J sandwich (Aldi's purchased peanut butter, grape jelly, white bread)
4-5 pm	10 Tysons brand Panko style Chicken nuggets, 6 cup Red Hawaiian Punch, Heinz ketchup
Note:	Chicken nuggets, Hawaiian Punch and Ramen Noodles are a staple in my diet.

Covid Considerations: This proposal is structured to have minimal person-to-person interactions. Though it might be constructive, I do not nrrd to enter the Wallens Ridge facility during the preliminary testing period. But a half day trip is required by NE with guards at least once to a medical center for SPECT/PET imaging. Repeating this with different dose levels of the challenge Red 40 or with a different imaging technique would be desirable but is not required.

References: Five references are attached in pdf format, plus many dozens more are given in downloadable pdf at ADHDBasics.info