

# Inflammation from Fat: The Name of the Brain Game

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## Abstract Body:

**Objective:** Demonstrate abnormal cerebral flow reserve in cognitively impaired insulin resistant (IR) patients and cerebral perfusion stimulation by coconut oil.

**Methods:** Brain SPECT indices of cerebral metabolism (CMi), perfusionj (CPi) and flow reserve FRi = CPi—CMi and FRr = (peak stimulated)/(basal counts/mCi used Tc-99m-HMPAO, basal and perfusion-stimulated with 0.8 mg nitroglycerin sl, 500 mg acetazolamide IV or 50 g coconut oil oral,. Omega 6:omega 3 ratio (O6O3R), Berkley Labs, was after > 12 hr fasting. Cognition wasw monitored with Test Your Memory (TYM).

**Results:** In 32 near normal patients age (51+-15) years, CMi was (57.0+-4.1)%, CPi (67.1+-4.9)%; FRi (10.2+-2.6)% and TYM 47.6+-1.5. In 47 cognitively impaired IR patients CMi was (53.8+-6.4)%, (p < 0.004); CPi (52.6+-11.7)%, (p< 0.002); FRi - (1.27+-12.4)%, (p < 0.0001) and TYM 35.7+-4.9, (p < 0.00001). Normalized FRi and FRr correlated in 43 cases with background , 27%, (r =0.93) using acetazolamide or nitroglycerin and similarly in 9 cases using coconut oil (r =0.92). By visual scan analysis, coconut oil often stimulated hypoperfused cortex preferentially. Moreover, in two caess, dietary manipulation, including two tablespoons (30 g) coconut oil daily, reduced O6O3R to 3.9 and 2.1 vs. the U.S. Population average of approximately 25:1.

**Conclusions:** Insulin resistant, cognitively impaired patients have abnormal cerebral flow reserve. Further studies will determine if anti-inflammatory fat therapy, such as decreasing the O6O3R, may have positive effects on abnormal cerebral function.

1.

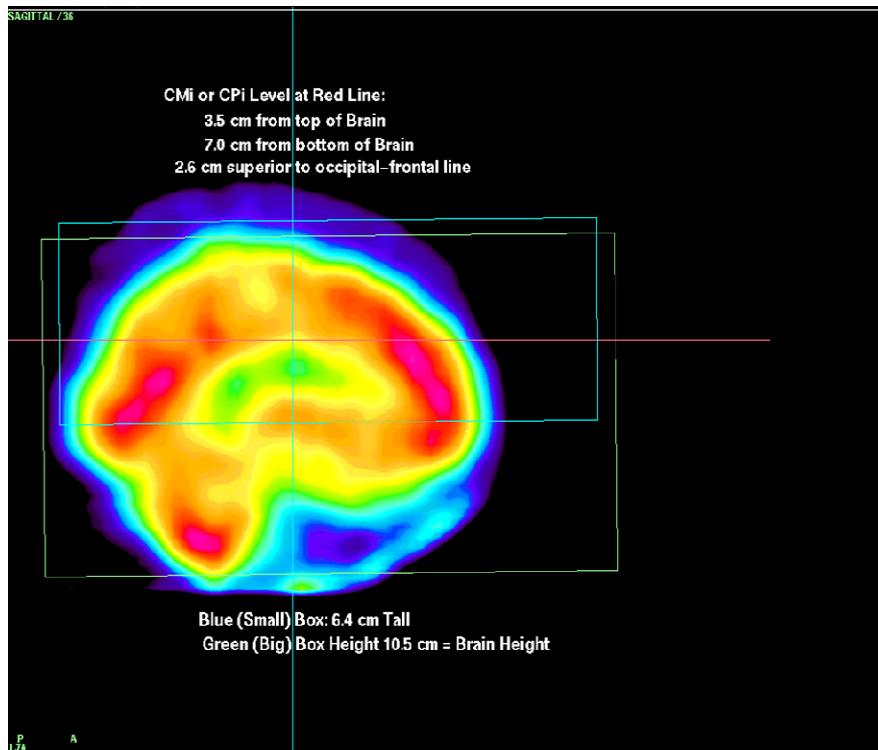


Fig. 1A. Axial SPECT slices are defined parallel to the brain long axis from occipital to prefrontal. For the Cortical Metabolic index (CMi), one or more axial slices are centered one third of the way from the top of the brain, just superior to the roof of the normalized lateral ventricles. Activity display uses a Sokoloff color scale, with white for peak brain, black for zero and spectral colors for intermediate activities. Computer-selected isocontours (see Fig. B) define areas that contain activity > a certain fraction of the peak activity. The 30% isocontour represents total brain activity in an axial slice, chosen slightly outside the actual external edge of the brain to correct for attenuation. The 60% isocontour approximates the cortex. The Cortical Metabolic index (CMi), the ratio of activity within the 60% isocontour to that within the 30% isocontour is a measure of cortical brain function. The Cortical Perfusion index (CPi) is similarly calculated from 60% and 30% isocontours after the patient receives a cerebral perfusion stimulant such as 0.5 to 1 g acetazolamide IV or 0.4 to 0.8 mg nitroglycerin sublingual. The difference between CPi and CMi is a measure of cerebral flow reserve (CFi).

<b>10.20</b>	<b>2.78</b>	<b>Normals</b>
<b>-5.93</b>	<b>25.81</b>	<b>Pituitary</b>
<b>0.3</b>	<b>12.93</b>	<b>Diabetics</b>
<b>1.17</b>	<b>11.01</b>	<b>Thyroid Disease</b>
<b>-0.5</b>	<b>19.00</b>	<b>Lo GFR</b>
<b>-2.24</b>	<b>22.81</b>	<b>Hi GFR</b>
<b>0.67</b>	<b>11.81</b>	<b>TBI</b>
<b>-0.06</b>	<b>13.79</b>	<b>IRS</b>

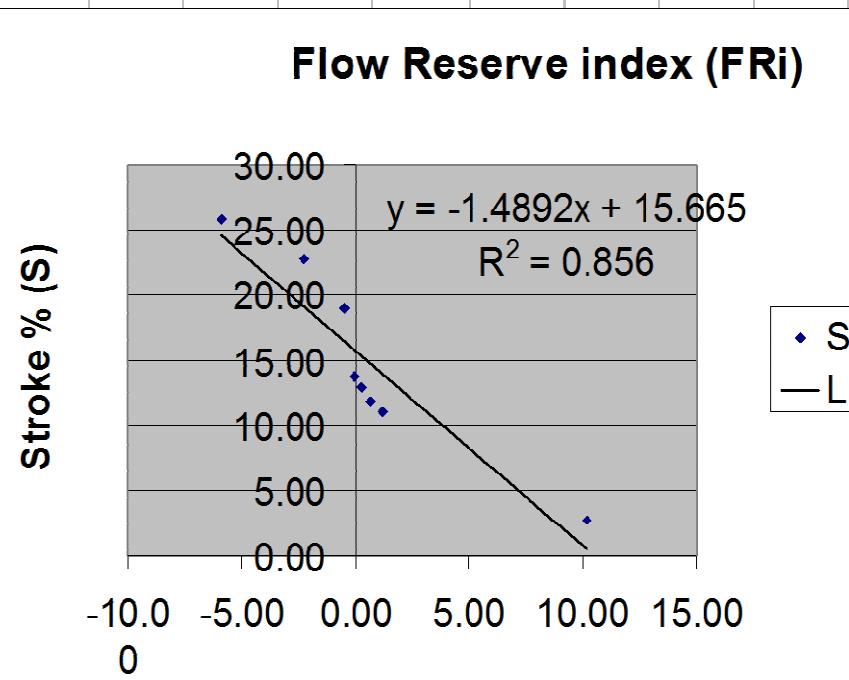


Fig 1B Graph of Flow Reserve Index (FRI) shown on the x axis above, vs. Stroke prevalence shown on the y axis above for 36 near normal patients age 52+14 years, with 2.77% stroke prevalence, for whom  $FRI = (10.2 \pm 2.6)\%$  and other interrelated groups. The post stroke Brain SPECT to the single near normal patient who eventually had a stroke is noted in Fig 2B to the right. The regression line is given by:

$$S = 15.67 - (1.49) FRI.$$

with correlation coefficient  $-0.925$ .

Parabolic renal corrections were employed but could be further optimized. Using GFR uncorrected for body surface area in part takes account of increased patient size increasing stroke incidence. The concept is that increased body size does not increase brain size but does increase risk of compromised cerebral circulation.

**2.**

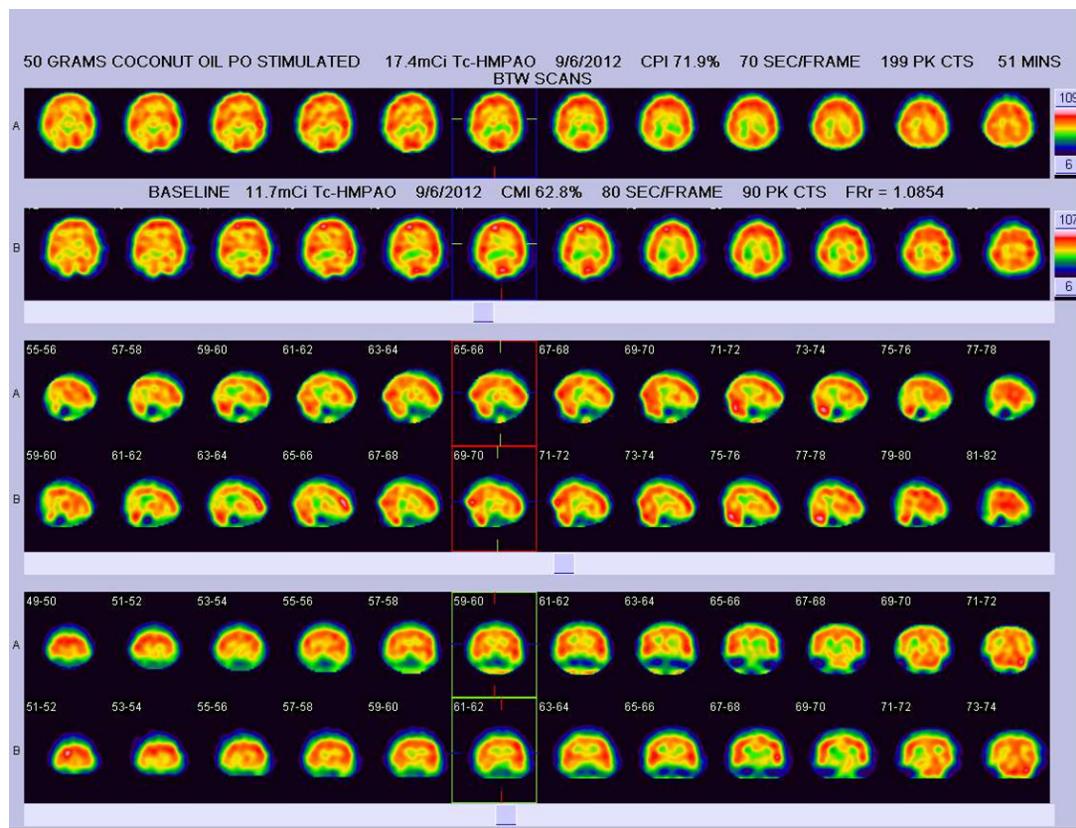
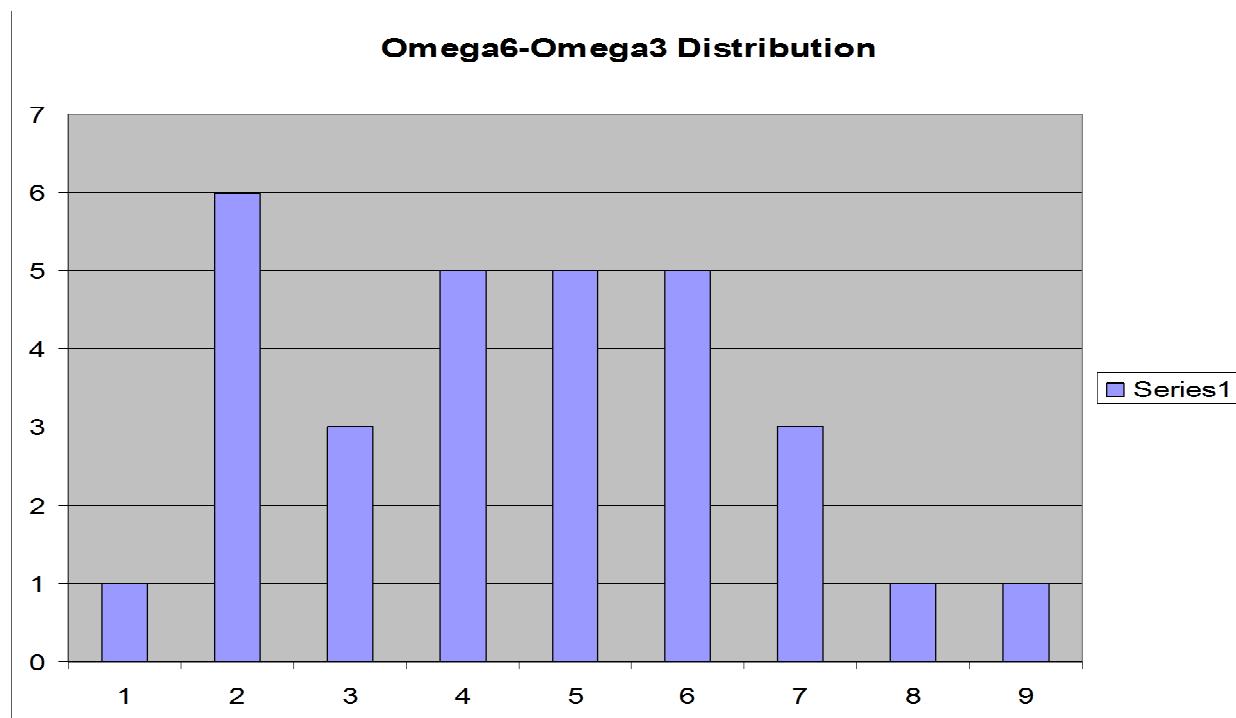


Fig 2A. Above: Near normal Brain SPECT for a 43 year old woman with migraine headaches using coconut oil as the perfusion stimulus. H.T. Pretorius et. al first reported that saturated fat stimulated brain perfusion using similar methods circa 2000.

Fig 2B. Below: Distribution plot of Omega6:Omega3 ratios for 31 individuals, age 61+-16 years, including 29 patients with either cognitive complaints or complications of insulin resistance and two of the authors who made specific dietary efforts to improve (decrease) their Omega6:Omega3 ratios. The modification efforts resulted in values of 3.9 and 2.1 which are toward the lower end of the patient distribution. All of the patients had been advised to follow a healthy diet, often including recommendation for fish oil supplements, and overall the ratios are lower than usually reported for the general population. Use of a single omega 6 reference (arachidonic acid) may have created some bias toward lower ratios in the Berkley Laboratory methods as compared to usual reported values. One diabetic patient on peritoneal dialysis had a low O6O3R of 1.7 but also a low out of range arachidonic acid value of 0.2 raising the question of whether arachidonic acid might be removed by peritoneal dialysis. All but two of the 7 values below 2.0 had out of range arachidonic Acid values 0.2 or less as did the lower of the two dietary modified values.



### 3.

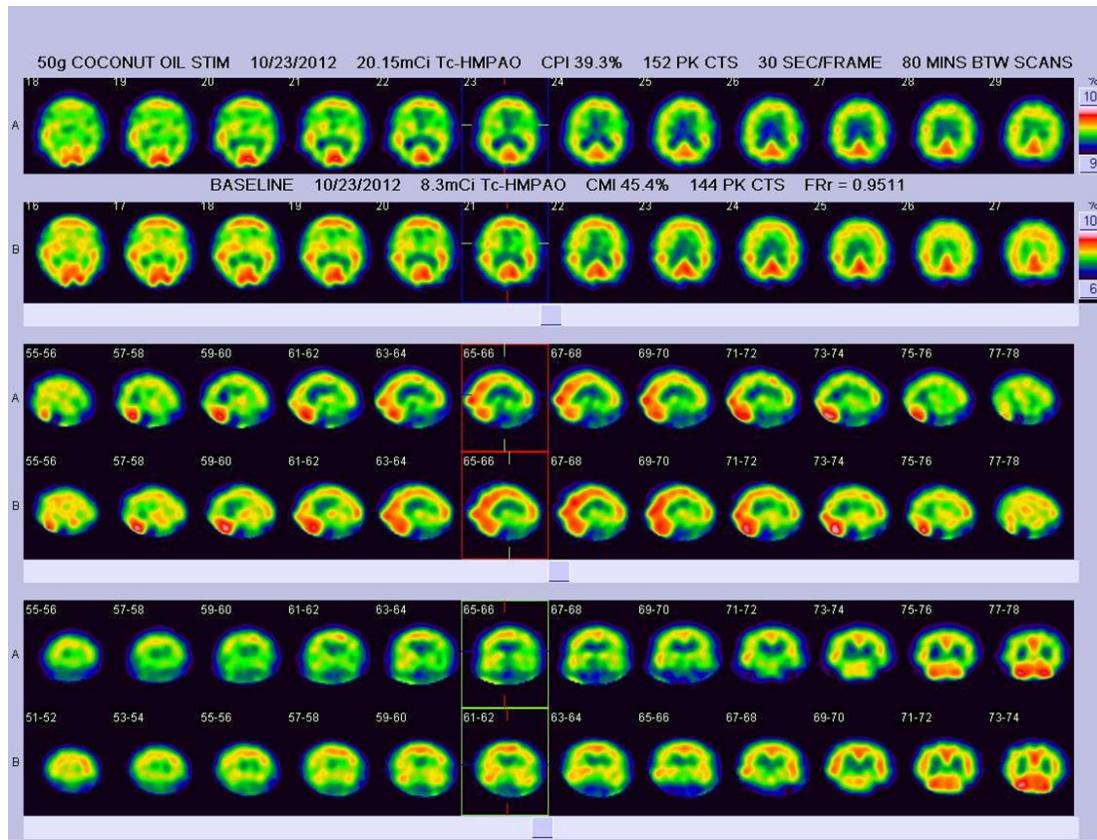
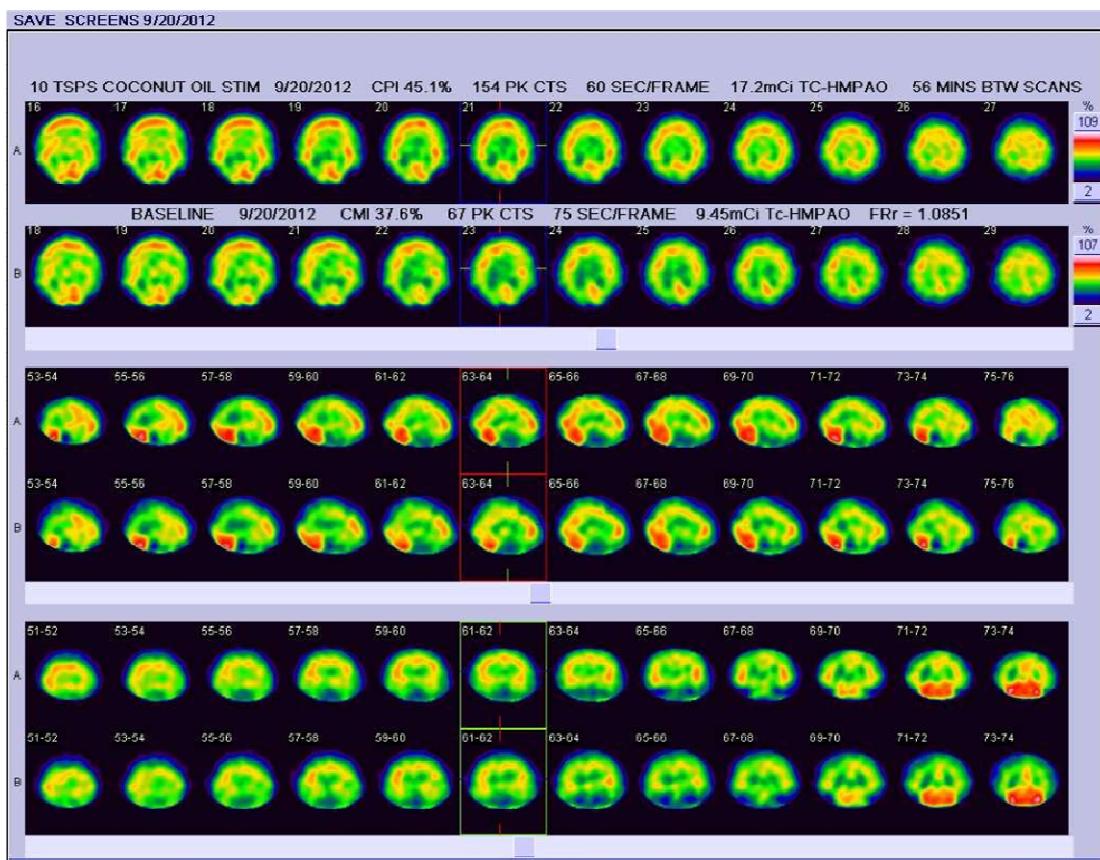


Fig. 3A. Above: Brain SPECT for a 75 year-old insulin resistant, hypertensive, hyperlipidemic, stage 2 chronic renal insufficent (eGFR 66 ml/min/1.73 meter sq), cognitively impaired (TYM 38) man showing low CMI of 45.4% vs. (57.0+-4.1)% noted in 32 near normal patients. The patient took over the counter fish oil but only in a dose of 1 gram daily and had history of a minor stroke 14 years earlier. We have seen no significant effects of such low-dose omega-3 supplements, which would be unlikely to make a significant impact on the O6O3R.

Fig. 3B. Below: Follow-up brain SPECT using coconut oil stimulus for a 62 year-old hypogonadal, hypertensive, nicotine dependent (> 60 pack year cigarette smoking) insulin resistant, cognitively impaired multiple sclerosis (MS) patient who refused and therapy for MS other than omega 3 fish oil increased from 1 gram daily to 4 grams daily after his first brain SPECT two years earlier (on 4-26-10). The initial brain SPECT using 0.8 mg nitroglycerin sl showed CMi 44.4% and CPI 41.8% with FRi = -2.6% while the follow-up SPECT showed CMi 37.6%, CPI 45.1% and FRi = 7.5%, consistent with interval improvement. The patient's family owns a Phillipine coconut plantation and he consumes coconut oil regularly.



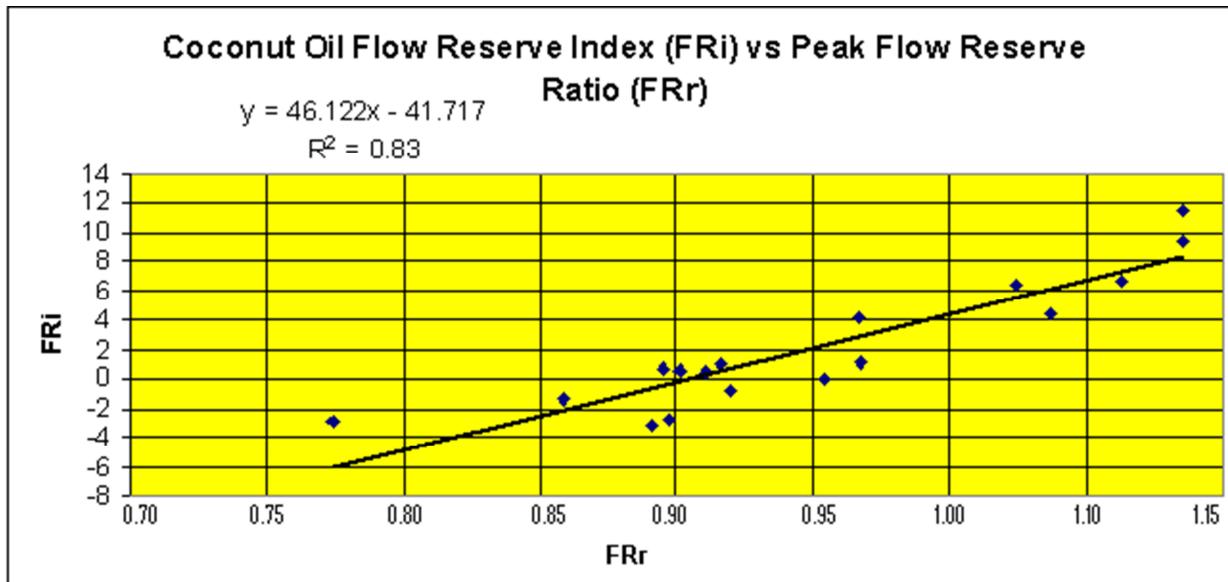
**4.**

Fig. 4A. Above: Graphical analysis of the Flow Reserve index (FRI), which depends primarily on activity near 65% of maximal, and the peak flow reserve ratio (FRr), which depends on the ratio of maximal stimulated vs. maximal basal activity per unit dose injected. With 17 points, including the near normal younger patient whose scan is shown in Fig 2A, the correlation coefficient 0.91 remains similar to 0.92 noted with the first 9 points in the abstract. The slope of the regression line above with coconut oil, 46.1, trended to be higher (9.5% higher) than the slope using routine perfusion stimulants, shown below, suggesting that coconut oil might stimulate intermediate areas of cerebral perfusion preferentially.

Fig. 4B. Below: Graphical analysis of the Flow Reserve index, (FRi) which depends primarily on activity near 65% of maximal, and the peak flow reserve ratio (FRr), which depends on the ratio of maximal stimulated vs. maximal basal activity per unit dose injected for usual perfusion stimulants, 0.8 mg sublingual nitroglycerin or 500 mg IV acetazolamide. With 38 points vs. 32 noted in the abstract, the correlation coefficient decreased from 0.93 to 0.87. The regression line slope of 42.1 tended to be lower than that of 46.1 noted in Fig 4A, above, using coconut oil as a perfusion stimulus.

