Supporting Information

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SI Text

Animal Preparation. Overnight-fasted Wistar rats (120–150 g) were anesthetized with 2–3% halothane in 30% O_2/67–68%N_2O, tracheotomized, and ventilated. The left femoral artery was cannulated for continuous monitoring of arterial blood pressure and intermittent sampling of blood for the measurement of glucose and gases. Both femoral veins were cannulated for the infusion of labeled substrates and the administration of either bicuculline (1 mg/kg dissolved in water, i.v.) or saline. Body temperature was maintained near 37 °C using a heating pad. In animals receiving bicuculline, a pair of carbon fiber leads were inserted in the scalp for monitoring electrocortical activity during the seizure, which was amplified, digitized, and recorded (Biopac Systems). Following surgery, halothane was reduced to ∼1% to sustain an adequate blood pressure. Before induction of seizures, animals were immobilized with D-tubocurarine chloride (initial dose of 0.25 mg/kg, i.p. with supplements of 0.10 mg/kg every 40 min). Blood was withdrawn (∼1.5 mL) into heparinized saline 2 min after the start of the glucose infusion to limit the peak rise in arterial blood pressure during the seizures and reinfused, as needed, to maintain blood pressure.

Infusion of FDG and [1,6-$^{13}C_2$]Glucose. The 2-Fluoro-2-deoxy-D-glucose (FDG, Sigma) and [1,6-$^{13}C_2$]glucose (Cambridge Isotopes; 99 atom%) were dissolved (molar ratio of 1:7) in deionized water (0.75 M per 200 g rat). The FDG/[1,6-$^{13}C_2$]glucose solution was infused as a bolus (0.27 mL in 15 s) followed by a stepped reduction in infusion rate every 30 s for the next 8 min (1), whereupon the rate was held constant until the time of decapitation. Pilot experiments with FDG infused for 8 min followed by decapitation showed that postmortem phosphorylation of FDG to FDG_{6P} occurred in the ischemic period following decapitation. Thus, to minimize postmortem FDG phosphorylation, the infusion of FDG was halted at 8 min, whereas the [1,6-$^{13}C_2$]glucose infusion was continued to 60 min. Plasma FDG levels declined rapidly after 8 min, comprising <3% of total plasma glucose at 60 min, thus minimizing the degree of postmortem phosphorylation. Thus, brain FDG_{6P} accumulation was proportional to the rate of glucose metabolism (glycolysis) in the interval preceding decapitation. In contrast, the ^{13}C labeling of amino acids had achieved their steady-state ^{13}C percentage enrichment at the time of decapitation.

In the seizure experiments, bicuculline was injected 2 min after the start of the FDG/^{13}C-glucose infusion to prelabel the brain glucose pool, minimizing ^{13}C label dilution of brain pyruvate by the expected rapid breakdown of unlabeled glucose and glycogen (2). Additional bicuculline was administered, as needed, to maintain electrographic seizure activity. In control animals not administered bicuculline, an equivalent volume of saline was injected 2 min after beginning the labeled [1,6-$^{13}C_2$]glucose infusion. Arterial blood samples were taken periodically for the analysis of plasma FDG/glucose concentration and label enrichment.

Preparation of Nerve Terminals. Nerve terminals were prepared from the forebrain (minus cerebellum) of rats using the method of Lai and Clark (3). A small amount (30 mg) of cortical tissue was also removed and frozen separately from each animal for the analysis of total FDG_{6P} and amino acids. Following decapitation, brains were removed quickly into a preweighed beaker containing ice-cold isolation medium (0.32 M sucrose, 10 mM Hepes, and 1 mM EDTA at pH 7.4), and weighed again to obtain brain weight. The volume of ice-cold medium was reduced and the brain chopped rapidly into small pieces, with frequent pauses to allow for heat dissipation. Residual blood in the solution was removed by decanting. Additional isolation medium was added (to final 1:10 vol/vol) and the brain was homogenized, and a small aliquot (1 mL) was removed and frozen to assess total homogenate FDG_{6P}. The homogenate was centrifuged at 1,300 × *g* for 3 min at 4 °C (Sorvall, SS-34 rotor), and the supernatant was collected. The pellet was resuspended in 10 mL of isolation medium, rehomogenized, and centrifugation repeated. The supernatants were pooled and recentrifuged at 17,000 × *g* for 10 min at 4 °C to pellet the crude mitochondrial fraction. The resulting pellet was resuspended in 15 mL of isolation medium and layered over a previously made discontinuous density gradient consisting of 11 mL of 7.5% (wt/wt) Ficoll 400 (dialyzed) solution over 11 mL of 10% (wt/wt) Ficoll 400 in Beckman Ultra-Clear thin wall (25 × 89 mm) centrifuge tubes. The resulting suspension was centrifuged in a Beckman SW 28 or Ti 32 rotor at 99,000 × *g* for 45 min (Beckman 5M ultracentrifuge). After ultracentrifugation, sample tubes revealed three bands: a white upper band at the boundary of isolation medium and 7.5% Ficoll medium, a white middle band at the 7.5%/10% (wt/wt) boundary consisting of nerve terminals, and a brown mitochondrial pellet. The myelin band and most of the 7.5% Ficoll layer were carefully removed. The nerve terminals were collected from the 7.5%/10% Ficoll interface and pelleted by centrifugation at 17,000 × *g* for 10 min at 4 °C (Sorvall, SS-34 rotor). Nerve terminal pellets were gently resuspended and pelleted twice in isotonic sodium chloride (1:5 vol/vol), resuspended in 1 mL final volume, and frozen in liquid nitrogen. Samples were stored at −80 °C until extracted.

Preparation of Extracts and NMR Analysis. Metabolites were extracted from nerve terminals and tissue homogenates using ice-cold ethanol (1:6 vol/vol; ethanol 60%, deionized water 40%). The [2-^{13}C]glycine (10 mM, 25 μL) and trifluoromethylalanine (TFMA, 10 mM, 25 μL; Lee's Bio-organic Laboratories) were added as internal concentration references. Suspensions were frozen and thawed several times to ensure complete cell lysis and centrifuged (20,000 × *g*). Extracts of cortical tissue (∼30 mg) were prepared as previously described (2) with addition of [2-^{13}C]glycine (10 mM, 50 μL) and TFMA (10 mM, 25 μL) as concentration references. The supernatants were lyophilized and resuspended in 500 μL of a phosphate-buffered (100 mM, pH7) deuterium oxide (Cambridge Isotopes) solution containing 0.25 mM 3-trimethylsilyl[2,2,3,3-D_4]-propionate as a chemical shift reference. The effective final concentrations of the [2-^{13}C]glycine and TFMA references were 1 mM and 0.5 mM, respectively.

NMR analysis of extracts. NMR spectra were measured on an 11.7 Tesla Bruker AVANCE spectrometer (Bruker Instruments) operating at 500.13 MHz for ^1H and 470.51 MHz for ^{19}F. FDG_{6P} was measured in extracts relative to trifluoromethylalanine (TFMA; Lee's Bio-organic Laboratories) using ^1H-decoupled ^{19}F NMR under nonrelaxed pulsing conditions (1-s interscan delay) and corrected for differential saturation of TFMA relative to FDG_{6P} and the relative number of fluorine atoms (3/1). The correction factor (0.865) was determined for a solution of FDG_{6P} (1 mM) and TFMA (1 mM) in 50 mM phosphate buffer at pH 7.0 (H_2O:D_2O, 85:15 vol%) by dividing the ratio FDG_{6P}/TFMA measured under fully relaxed conditions without ^1H decoupling (0.366) by that measured under the rapid pulsing conditions with ^1H decoupling (0.423). Total plasma FDG and brain FDG_{6P} concentrations were determined by measurement of the α anomer divided by the α anomer equilibrium fraction [α/β = 0.44/0.63 (4)]. In extracts of brain tissue, nerve terminals and homogenate, FDG

and FDG_{6P} were determined as the sum of the resolved C1 α and β anomers.

Amino acid concentrations were determined with ^{1}H-[^{13}C]-NMR under fully relaxed conditions (20-s interscan delay) as described in de Graaf et al. (5). The *N*-acetylaspartate (NAA) acetyl methyl and ^{13}C-labeled glycine methine protons were measured from the respective peak areas of the ^{1}H-[^{13}C]-NMR spectra reflecting total $^{12}C+^{13}C$ covalently bound ^{1}H (NAA) or ^{13}C bound ^{1}H resonances ([2-^{13}C]glycine).

Analysis of plasma FDG and glucose. FDG and glucose were measured from arterial blood plasma sampled periodically during experiments. Plasma glucose was measured with a Glucose Analyzer II (Beckman Instruments). For NMR measurements, plasma was mixed with deuterium oxide and passed through a centrifugal filter (10 kDa cut off, Nanosep, Gelman Laboratory) to remove macromolecules (14,000 × *g*). The FDG mole fraction in plasma was calculated by dividing the FDG-$C1_\alpha$ resonance intensity by the total (FDG + glucose)-$C1_\alpha$ intensity.

Assessment of Nerve Terminal Purity. ***Protein Determination for Immunoblotting.*** Protein concentrations in samples were determined, following protein precipitation using the Compat-Able Protein Assay Preparation Reagent Set (Pierce), by a bicinchoninic acid method using BSA as a protein standard (BCA Protein Assay Kit, Pierce). Equal amounts of protein (15 μg) were mixed with an equal volume of 1× loading buffer containing 8 M urea, 62.5 mM Tris (pH 6.8), 2% SDS, 20% glycerol, and 0.2% bromophenol blue.

Immunoblotting. Immunoblotting for glial fibrillary acidic protein (GFAP) and β-actin (loading control) was performed using commercially available primary antibodies and HRP-coupled secondary antibodies with chemiluminescence detection on standard X-ray film. Briefly, equal amounts of total protein (10 μg) were loaded and separated by polyacrylamide gel electrophoresis on 4–20% gradient gels (Criterion, Bio-Rad) and transferred onto nitrocellulose membranes (Biotrace NT, Pall Life Sciences). Nonspecific binding sites were blocked (5% skimmed milk in 10 mM Tris pH 7.5, 37.5 mM sodium chloride, and 0.5% Tween-20) and membranes were incubated for 1 h with antibodies directed against GFAP or β-actin (Santa Cruz Biotechnology). After repeated washings, the membranes were incubated overnight (GFAP) or for 1 h (actin) with an appropriate species-specific secondary antibody. GFAP and actin were detected by enhanced chemiluminescence following exposure to photographic film (Kodak X-Omat AR). The films were digitized (Linoscan 1400) and stored as tagged image file format images for analysis using ImageJ (6). GFAP optical densities were expressed as the ratio with β-actin.

Glutamine synthetase assay. Glutamine synthetase (GS) activity was measured in the synthetase (Glu + ATP + NH_2OH) direction using a modification of the assay of Petito et al. (7) to accommodate use of a plate reader. Nerve terminals, brain homogenate, or cortical tissues were homogenized in 10 volumes of ice-cold 0.15M KCl using a glass homogenizer. Homogenate (100 μL; 10:1 v/w) was incubated for 15 min at 37 °C with 0.2 mL of a reaction mixture containing 50 mM glutamate, 100 mM imidazole-HCL buffer (pH 7.4), 10 mM β-mercaptoethanol, 10 mM $MgCl_2$, 50 mM hydroxylamine (pH 7.4), and 10 mM ATP. After 15 min, the reaction was stopped by addition of 0.8 mL of a solution containing 0.37 M ferric chloride, 0.2 M trichloroacetic acid, and 0.67 M HCl, and centrifuged. The supernatant was incubated for 15 min at room temperature and the colored reaction product, γ-glutamyl hydroxamate, was measured at 540 nm using a 96-well plate reader (Biotek Instruments; KC-4 v.3 software) and compared with standard quantities of pure γ-glutamyl hydroxamate treated with $FeCl_2$ reagent.

Incubation of isolated nerve terminals with ^{13}C-labeled substrates. Metabolic ^{13}C labeling assays were conducted to assess potential contamination of nerve terminals by intact astroglia. The nerve terminals were diluted with isotonic medium (1:5) and were incubated with either [2-^{13}C]acetate (12 μL; 100 mM) or [1,6-$^{13}C_2$] glucose (30 μL; 100 mM) plus [U-$^{13}C_5$]glutamate (6 μL; 20 mM) for 15 min and 30 min. At the end of the incubation period, the nerve terminal suspensions were centrifuged at 17,000 × *g* for 10 min at 4 °C. Both the pellet and supernatant were frozen in liquid N_2 and stored separately at −80 °C. In addition, aliquots of brain tissue homogenates from the nerve terminal preparations were also incubated with the same ^{13}C-labeled substrates described above.

Effects of Astroglial Glucose Oxidation on Predicted Neuronal Glucose Uptake. As discussed in Hyder et al. (8), the 1:1 relationship between ΔV_{cyc} and $\Delta 0.5V_{TCAn}$ allows for direct neuronal glucose uptake to the extent that glucose uptake in astrocytes (stimulated by glutamate uptake) is oxidized there, rather than releasing lactate for export to neurons. In this case, the predicted neuronal glucose phosphorylation and oxidation in neurons can be computed as

$$CMRglc_n^{(P+Ox)} = 0.5*V_{TCAn} - \left(V_{cyc} - \left[CMRglc_{(ox)a} - CMRglc_{(ox)a}^{(iso)}\right]\right), \quad \textbf{[S1]}$$

where $[CMRglc_{(ox)a} - CMRglc_{(ox)a}^{(iso)}]$ represents the magnitude of activity-dependent astrocytic glucose oxidation above isoelectricity, effectively reducing the supply of pyruvate (lactate) available for transfer to neurons. Substitution of $CMRglc_{(ox)a} = 0.5*(V_{PDHa} + V_{PC})$ and $CMRglc_{(ox)a}^{(iso)} = 0.5*(V_{PDHa} + V_{PC})^{(iso)}$ in Eq. **S1** gives

$$CMRglc_n^{(P+Ox)} = 0.5*V_{TCAn} - \left(V_{cyc} - \left[0.5*(V_{PDHa} + V_{PC}) - 0.5*(V_{PDHa} + V_{PC})^{(iso)}\right]\right), \quad \textbf{[S2]}$$

where V_{TCAn} is the neuronal tricarboxylic acid (TCA) cycle flux, V_{PDHa} is the astroglial pyruvate dehydrogenase flux, and V_{PC} is the astroglial pyruvate carboxylase flux. Using estimates of astrocyte oxidation and other fluxes with activity as given in Table 2 (legend) with Eq. **S2**, the predicted $CMRglc_n^{(P+Ox)}$ for the seizure condition would be ~0.11 μmol·g^{-1}·min^{-1}, which is ~38% above the value of 0.08 μmol·g^{-1}·min^{-1} predicted for model 1 under the assumption that astroglial oxidation is unchanged by the increased activity (Table 2). Higher values of astroglial glucose oxidation than assumed here would lead to correspondingly more glucose uptake in neurons (8, 9) to satisfy their oxidative needs.

The expression, $0.5*(V_{PDHa} + V_{PC})$ in Eq. **S2**, is equal to the rate of astroglial oxidation, $CMRglc_{(ox)a}$. From Gruetter et al. (10):

$$CMRglc_{(ox)a} = \left(V_g^{TCA} + V_{PC}\right)/2, \quad \text{where } V_g^{TCA} = V_g + V_{PC} \text{ and } V_g = V_{PDHa} - V_{PC},$$

which, after substitution of V_g^{TCA} and rearrangement, becomes

$$CMRglc_{(ox)a} = \left(\left(V_g + V_{PC}\right) + V_{PC}\right)/2 = \left(V_g + 2V_{PC}\right)/2 = V_g/2 + V_{PC}. \quad \textbf{[S3]}$$

With substitution of V_g (= $V_{PDHa} - V_{PC}$) in Eq. **S3**,

$$CMRglc_{(ox)a} = (V_{PDHa} - V_{PC})/2 + V_{PC} = (V_{PDHa} + V_{PC})/2. \quad \textbf{[S4]}$$

Eq. **S4** appears in Eqs. **2** and **5** and Table 2 legend.

1. Fitzpatrick SM, Hetherington HP, Behar KL, Shulman RG (1990) The flux from glucose to glutamate in the rat brain in vivo as determined by ^{1}H-observed, ^{13}C-edited NMR spectroscopy. *J Cereb Blood Flow Metab* 10(2):170–179.
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4. Oberdorfer F, Hull WE, Traving BC, Maier-Borst W (1986) Synthesis and purification of 2-deoxy-2-[^{18}F]fluoro-D-glucose and 2-deoxy-2-[^{18}F]fluoro-D-mannose: Characterization of products by ^{1}H- and ^{19}F-NMR spectroscopy. *Int J Rad Appl Instrum [A]* 37(8):695–701.
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9. Jolivet R, Magistretti PJ, Weber B (2009) Deciphering neuron-glia compartmentalization in cortical energy metabolism. *Front Neuroenergetics* 1:4.
10. Gruetter R, Seaquist ER, Ugurbil K (2001) A mathematical model of compartmentalized neurotransmitter metabolism in the human brain. *Am J Physiol Endocrinol Metab* 281(1):E100–E112.

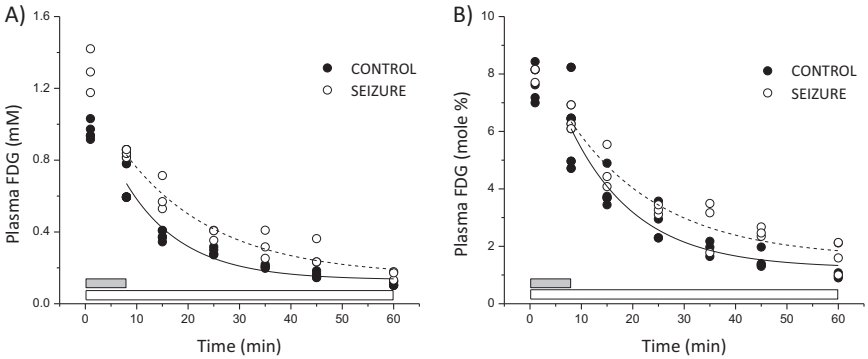

Fig. S1. Time courses of plasma FDG washout in control and seizure groups following an 8-min infusion of FDG. (*A*) Plasma FDG concentration (millimolars). (*B*) Plasma FDG mole fraction (%). FDG (solid bar) and [1,6-$^{13}C_2$]glucose (open bar) were infused together for 8 min, after which the infused solution was switched to one containing ^{13}C-glucose only, maintaining a constant glucose concentration and ^{13}C isotopic enrichment. A monoexponential decay function (solid line, Control; dashed line, Seizures) was fitted to data from 8 min to 60 min for each group to determine FDG washout kinetics and FDG mole fraction × time integrals. The total integrals (FDG mole % × min) were evaluated from 0 to 60 min for each animal and the group averages calculated (control/seizure ratio = 0.853). The brain FDG_{6P} concentrations measured in the seizure animals was multiplied by 0.853 to adjust for differences between groups in the integrated blood FDG mole fractions. The application of this normalization assumes that the rate of brain FDG_{6P} formation is proportional to blood FDG mole fraction.

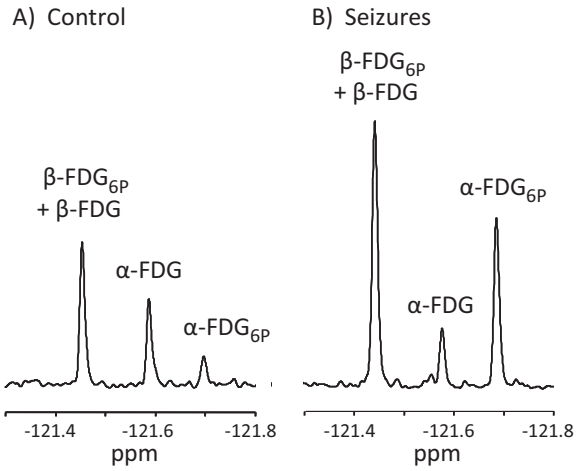

Fig. S2. The ^{19}F NMR spectra of nerve terminal extracts prepared from the brains of rats decapitated at 8 min following FDG/glucose infusion and seizure induction without the washout. Nerve terminals were prepared from the brain homogenate as described in *Materials and Methods*. (*A*) Control, (*B*) Bicuculline-induced seizures. Relatively high free FDG is visible in the spectra, which, in the control, accounts for the majority of the β-FDG peak. A washout period was included in the experimental protocol to reduce potential postmortem metabolism of free FDG to FDG_{6P} during terminal preparation.

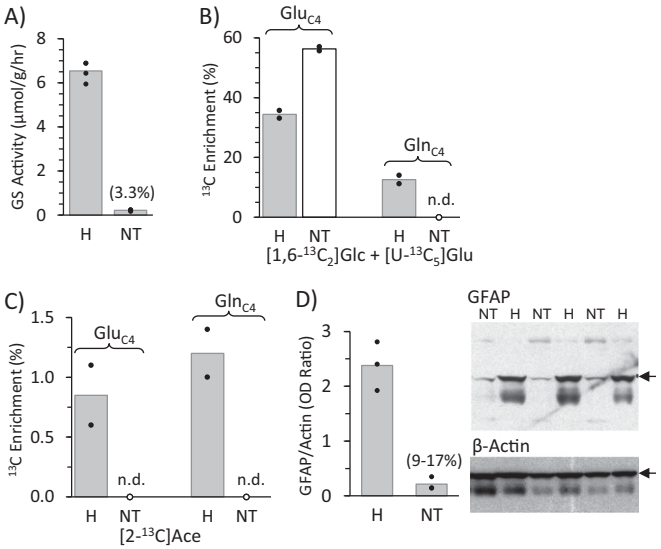

Fig. S3. Assessment of glial contamination of isolated nerve terminals. (*A*) Glutamine synthetase (GS) activity in brain homogenate (H) versus nerve terminals (NT). GS activity in nerve terminals was ~3.3% of homogenate. Bar graph reflects average values of four different preparations each consisting of four rat brains (NT, 0.217 vs. H, 6.54 $\mu mol \cdot h^{-1} \cdot g^{-1}$). (*B* and *C*) Results of incubation of nerve terminals and total brain homogenate ($n = 2,2$) with ^{13}C-labeled precursors in vitro, [U-$^{13}C_5$]glutamate (Glu) + [1,6-$^{13}C_2$]glucose (Glc) (*B*) or [2-^{13}C]acetate (Ac) (*C*) depicting excess ^{13}C percentage enrichment above the 1.1% natural abundance of carbon 4 (C4) of Glu_{C4} and Gln_{C4}. Glutamine labeling was detected in homogenate but not in nerve terminals. (*D*) Immunoblot of GFAP in nerve terminals and brain homogenate with β-actin as loading control (10 μg protein/lane). Major bands for GFAP (~50 kDa) and β-actin shown by horizontal arrows; broader, faster running bands below are presumably degradation products. GFAP in nerve terminals (as % of homogenate) ranged from ~9% (OD of both GFAP bands) to 17% (OD of GFAP major band only). Bar graph reflects average of three separate preparations each consisting of three to four rat brains.

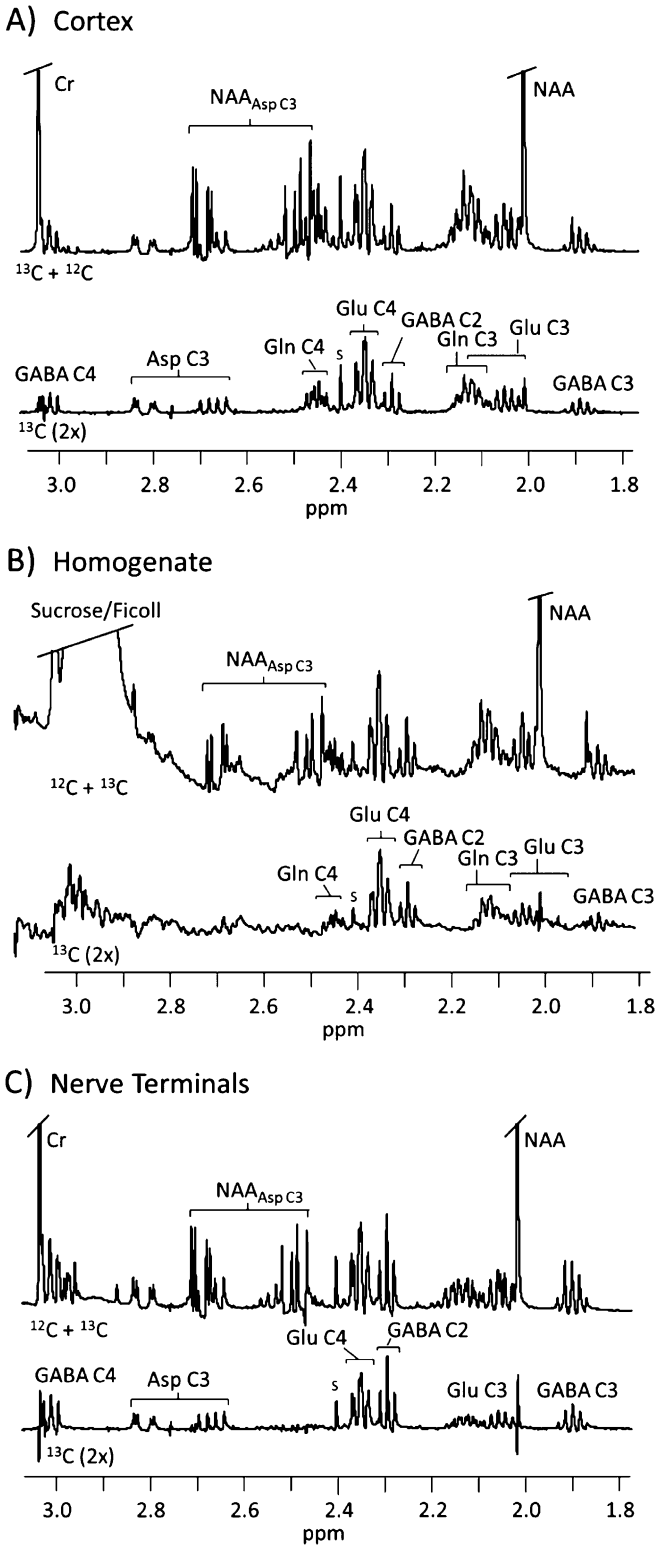

Fig. S4. The ^{1}H-[^{13}C] NMR spectra of (*A*) cortex, (*B*) whole brain homogenate, and (*C*) nerve terminal extracts following a 60-min [1,6-$^{13}C_2$]glucose infusion before decapitation, brain removal, and tissue fractionation. Nerve terminals were prepared from the brain homogenate as described in *Materials and Methods*. Whereas glutamine is readily seen in extracts of cortex and whole brain homogenate, glutamine was not detected in nerve terminals, consistent with other assessed markers indicating relatively low glial contamination. The spectral distortion in the downfield region of the homogenate is due to the residual sucrose and Ficoll used in the fractionation. The high ^{13}C enrichment of glutamate and GABA confirmed that the nerve terminals had been actively oxidizing ^{13}C-glucose (or its product ^{13}C-lactate) at the time of FDG phosphorylation. Vertical amplitudes for creatine (Cr), *N*-acetylaspartate (NAA), and sucrose/Ficoll were truncated for clarity.

Table S1. Average plasma concentrations of glucose, FDG, and FDG mole fraction in control and seizure groups for the period of 1–8 min and at 60 min

		Time, minutes of infusion		
	Condition	0	1–8 min*	60 min[†]
Glucose (mM)	control	5.9 ± 0.7	10.4 ± 1.1	9.6 ± 4.3
	seizure	5.4 ± 0.9	13.6 ± 1.0[‡]	10.6 ± 2.4
FDG (mM)	control	0	0.82 ± 0.06	0.12 ± 0.01
	seizure	0	1.07 ± 0.05[§]	0.16 ± 0.03
FDG (mole % of total)	control	0	7.3 ± 0.7	1.4 ± 0.6
	seizure	0	7.2 ± 0.3	1.6 ± 0.6

Whereas significant increases were observed in glucose and FDG concentrations during seizures for the 1- to 8-min period, the FDG mole percentage was unchanged at either time period (1–8 min, $P > 0.4$; 60 min, $P > 0.7$).
*Average value of 1–8 min.
[†]FDG infusion was halted at 8 min while [1,6-$^{13}C_2$]glucose infusion continued followed by sacrifice and nerve terminal preparation at 60 min; in the time period from 8 to 60 min, plasma FDG levels declined monotonically (see Fig. S1). Glucose reflects total concentration, $^{12}C + {}^{13}C$. FDG mole fraction of total glucose (percent) is given by FDG/(FDG + glucose) × 100 and was calculated for individual animals. Values are mean ± SD of three different preparations under control and seizure conditions.
[‡]Control vs. seizure: $P < 0.05$.
[§]Control vs. seizure: $P < 0.01$.

Table S2. FDG_{6P} expressed as a ratio with different neuron-enriched metabolites

	Control		Seizures	
Ratio	Nerve term.	Homogenate	Nerve term.	Homogenate
FDG_{6P}/NAA	0.045 (±0.007)	0.046 (±0.010)	0.093 (±0.015)	0.086 (±0.012)
$FDG_{6P}/(Glu_4+GABA_2)_{ss}$	0.149 (±0.042)	0.149 (±0.037)	0.280 (±0.048)	0.388 (±0.022)
FDG_{6P}/(Glu+GABA)	0.035 (±0.011)	0.033 (±0.008)	0.069 (±0.011)	0.073 (±0.008)

Values are mean (± SD) of three different preparations under control and seizure conditions. The concentration of FDG_{6P} was quantitated as the sum of the resolved α and β anomer peaks in the ^{19}F NMR spectrum according to the following formula: $[FDG_{6P}] = FDG_{6P}(\alpha + \beta) \times 1/A \times 1/B \times 3/1 \times C$, where A is the correction for saturation due to incomplete T1 relaxation (0.866), B is the concentration of the reference (TFMA) equal to 0.5 mM, 3/1 corrects for differences in the number of fluorine atoms in TFMA (3) and FDG_{6P} (1), and C is a normalization factor to correct for between-group differences in the mole fraction (percent) versus time integrals of the curves shown in Fig. S1 and described in the legend. FDG_{6P}, fluoro-deoxy-D-glucose-6P; $GABA_2$, gamma-aminobutyrate-$^{13}C2$; Glu_4, glutamate-$^{13}C4$; NAA, *N*-acetylaspartate; Nerve term., nerve terminal; subscript *ss*, steady-state ^{13}C concentrations.

Table S3. Comparison of seizure-to-control ratios of cortical FDG_{6P}/NAA and in vivo glucose utilization

Seizure-to-control ratio (cortex)			
Ex vivo*	In vivo[†]		
FDG_{6P}/NAA	$CMRglc_{(ox)n}$	$CMRglc_{(ox)tot}$	$CMRglc_{(tot)}$
2.6*	2.19	2.0	4.7[‡], 2.8[§]

*Present study, reflects the cortical ratio of FDG_{6P}/NAA values for seizure (0.097) and control (0.037) conditions. A small piece of cerebral cortex was removed before homogenization.
[†]In vivo values reflect changes in the cerebral metabolic rate of neuronal or total glucose oxidation and total glucose utilization ($CMRglc_{(ox)n}$, $CMRglc_{(ox)tot}$, $CMRglc_{(tot)}$), respectively, reported by Patel et al. (2).
[‡]Values refer to seizure onset conditions.
[§]Values refer to steady-state conditions.