BIOGRAPHICAL SKETCH

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NAME: Stephen C. CUNNANE	POSITION TITLE: Full Professor
eRA COMMONS USER NAME	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Bishop's University, Quebec, Canada	BSc	05/75	Biopsychology
Bishop's University, Quebec, Canada	BEd	05/76	Education
McGill University, Montreal, Canada	PhD	05/80	Physiology
Rowett Research Institute, Aberdeen, UK	Post-doc	06/80-06/81	Nutritional Biochemistry
Institute of Zoology, London, UK	Post-doc	07/81-06/82	Lipid Biochemistry
Efamol Research Institute, Nova Scotia, Canada	Post-doc	07/82-09/86	Lipid Biochemistry

Personal Statement

Over the past 12 years my research group has developed positron emission tomography (PET) and magnetic resonance imaging (MRI) methods to quantify brain fuel metabolism during aging and in those at risk of Alzheimer's disease (AD). We have the only PET center worldwide with the capability to measure ketone metabolism in clinical studies (using carbon-11-acetoacetate). This program was undertaken with the financial support of the Quebec and Canadian governments and my Research Chair (initially Canada Research Chair follows by a University Research Chair). It is a collaborative project involving physiologists, neuroimaging specialists, neurologists and geriatricians. We have shown that cognitively normal older persons have 8-12% lower uptake of glucose (FDG) in specific brain regions but that brain ketone uptake is unchanged relative to young healthy adults. Hence, brain glucose hypometabolism can precede cognitive decline and appears to be specific to glucose.

We quantify uptake of both brain fuels (glucose [as FDG] and ketones as 11C-acetoacetate), so we know the actual magnitude of the deficit when it occurs. Although other groups have also reported on brain FDG uptake during aging, most groups use a simpler PET protocol that only permits statistical assessment of the difference between groups and not the actual magnitude of the difference in fuel uptake. This distinction is important because without quantification, one cannot determine the target amount of ketones that would be needed to correct or bypass the brain's glucose uptake deficit. Ketones are pertinent because – (i) they are the brain main back-up fuel to glucose, (ii) they have beneficial effects on cognition and, (iii) their brain uptake is unchanged in cognitively healthy elderly and in early Alzheimer's disease (see Nugent et al 2014, Castellano et al 2015; Publication list).

Positions

2003-	Full Professor, Université de Sherbrooke, Sherbrooke, Quebec, Canada
2003-	Researcher, Research Center on Aging, Université de Sherbrooke
2007-2009	Director, Research Center on Aging, Sherbrooke
1986-2003	Assistant, Associate, Full Professor, University of Toronto, Toronto, Canada

Honours

2007-	Seven publications have won prizes or were the journal's top-cited papers
2011-2018	University of Sherbrooke Research Chair in Brain Metabolism and Aging
2011	Etienne LeBel Prize (Université de Sherbrooke; outstanding career contributions)
2010	Jean de Margerie Prize (Université de Sherbrooke; top clinical publication in 2009)
2009	National Academy of Medicine, France (1 of only 100 foreign members worldwide)
2003-2010	Senior Canada Research Chair in Brain Metabolism and Aging
1995	Outstanding Scientist award, Canadian Society for Nutritional Sciences

Refereed Papers (♦ prize winning papers)**:**

Provencher D, Hennebelle M, **Cunnane SC**, Bérubé-Lauzière Y, Whittingstall K. Cortical thinning in healthy aging correlates with larger motor-evoked EEG desynchronization. Frontiers in Aging Neurosci, accepted March 7, 2016.

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Castellano CA, Baillargeon JP, Nugent S, Tremblay S, Fortier M, Imbeault H, Duval J, **Cunnane SC**. Regional Brain glucose hypometabolism in young women with polycystic ovary syndrome: possible link to mild insulin resistance. PLoS One. 2015 Dec 9;10(12):e0144116.

Fulop T, Dupuis G, Baehl S, Le Page A, Bourgade K, Frost E, Witkowski JM, Pawelec G, Larbi A, **Cunnane SC**. From inflamm-aging to immune-paralysis: a slippery slope during aging for immune-adaptation. Biogerontology. 2015 Oct 15. [Epub ahead of print] PMID:26472173.

Noll C, Kunach M, Frisch F, Bouffard L, Dubreuil S, Jean-Denis F, Phoenix S, **Cunnane SC**, Guérin B, Turcotte EE, Carpentier AC. Seven-Day Caloric and Saturated Fat Restriction Increases Myocardial Dietary Fatty Acid Partitioning in Impaired Glucose-Tolerant Subjects. Diabetes. 2015 Nov;64(11):3690-9.

Pifferi F, Dorieux O, Castellano CA, Croteau E, Masson M, Guillermier M, Van Camp N, Guesnet P, Alessandri JM, **Cunnane SC**, Dhenain M, Aujard FG. (2015). Dietary omega-3 polyunsaturated fatty acids enhance resting state brain glucose utilization and reduce anxiety in an adult non-human primate, the grey mouse lemur (*Microcebus murinus*). Journal of Lipid Research 56, 1511-18.

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Nugent S, **Cunnane SC**. (2015). Medium chain fatty acids and infant brain development: Implications for the problem of deteriorating brain glucose metabolism during aging. Oléageneux, Corps Gras et Lipides. In press.

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Roy M, Beauvieux MC, Naulin J, El Hamrani D, Gallis JL, Cunnane SC, Bouzier-Sore AK. (2015). Rapid adaptation of rat brain and liver metabolism on a ketogenic diet: an integrated study using 1H- and 13C-NMR spectroscopy. J Cerebral Blood Flow Metabolism, e-pub. PMID 25785828

Cunnane SC. (2015). Contraintes énergétiques et nutritionnelles sur le développement du cerveau: Implications pour l'expansion du cerveau humain au cours de son évolution. Cahiers de Nutrition, in press.

Hennebelle M, Harbeby E, Tremblay S, Chouinard-Watkins R, Pifferi F, Plourde M, Guesnet P, **Cunnane SC**. (2014). Challenges to determining whether DHA can protect against age-related cognitive decline. Clinical Lipidology, accepted March 2, 2015.

Castellano CA, Nugent S, Paquet N, Tremblay S, Bocti C, Lacombe G, Imbeault H, Turcotte É, Fulop T, **Cunnane SC**. (2015). Lower brain 18F-fluorodeoxyglucose uptake but normal 11C-acetoacetate metabolism in mild Alzheimer's disease dementia. Journal of Alzheimer's Disease. 43(4): 1343-1353.

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Pélerin H, Jouin M, Lallemand MS, Alessandri JM, **Cunnane SC**, Langelier B, Guesnet P. (2014). Gene expression of fatty acid transport and binding proteins in the blood-brain barrier and the cerebral cortex in the developing rat with different DHA brain status. PLEFA 91, 213-220.

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Hennebelle, M., Plourde, M., Chouinard-Watkins, R., Castellano, C.-A., Barberger-Gateau, P., & **Cunnane, S. C.** (2014). Aging and apo E change DHA: relevance to age-related cognitive decline. Proc Nutr Soc*,* 73, 80-86.

Plourde, M., Chouinard-Watkins, R., Rioux-Perreault, C., Fortier, M., Dang, M.T., Allard, M.J., Tremblay-Mercier, J., Zhang, Y., Lawrence, P., Vohl, M.C., Perron, P., Lorrain, D., Brenna, J.T., **Cunnane, S. C.** (2014). Kinetics of ^{13}C-DHA before and during fish-oil supplementation in healthy older individuals. Amer J Clin Nutr 100, 105-112.

Roy, M., Nugent, S., Tremblay, S., Descoteaux, M., Beaudoin, J.F., Tremblay, L., Lecomte, R., **Cunnane, S.C**. (2013). A dual tracer PET-MRI protocol for the quantitative measure of regional brain energy substrates uptake in the rat. J Visual Exp, Dec 28;(82):50761. doi: 10.3791/50761

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Umhau, J. C., Zhou, W., Thada, S., Demar, J., Hussein, N., Bhattacharjee, A. K., Ma, K., Majchrzak-Hong, S., Herscovitch, P., Salem Jr, N., Urish, A., Hibbeln, J. R., **Cunnane, S. C.**, Rapoport, S. Il, & Hirvonen, J. (2013). Brain docosahexaenoic acid incorporation and blood flow are increased in chronic alcoholics: a PET study corrected for cerebral atrophy. PLOS One*,* 8(10), e75333.

Cunnane, S. C., Schneider, J. A., Tangney, C., Tremblay-Mercier, J., Fortier, M., Bennett, D. A., & Morris, M-C. (2012). Plasma and brain fatty acid profiles in mild cognitive impairment and Alzheimer's disease. Journal of Alzheimer's Disease*,* 29(3), 691-697.

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Plourde, M., Chouinard-Watkins, R., Vandal, M., Zhang, Y., Lawrence, P., Brenna, J. T., & **Cunnane, S. C.** (2011). Plasma incorporation, apparent retroconversion and beta-oxidation of 13C-docosahexaenoic acid in the elderly. Nutrition and Metabolism, 8, 1-9.

Croteau, E., Lavallée, E., Ménard, S. L., Hubert, L., Pifferi, F., Rousseau, J., **Cunnane, S. C.**, &. Carpentier, A. D. (2010). Image-derived input function in dynamic human PET/CT: methodology and validation with 11C-acetate and 18F-fluorothioheptadecanoic acid in muscle and 18F-fluorodeoxyglucose in brain. European Journal of Nuclear Medicine and Molecular Imaging, 37(8), 1539-1550.

D'Asti, E., Long, H., Tremblay-Mercier, J., **Cunnane, S. C.**, di Marzo, V., & Walker, C-D. (2010). Maternal dietary fat determines metabolic profile and the magnitude of endocannabinoid inhibition of the stress response in neonatal rat offspring. Endocrinology, 151(4), 1685-1694.

Fortier, M., Plourde, M., Vandal, M., Pifferi, F., Tremblay-Mercier, J., Freemantle, E., & **Cunnane, S. C.** (2010). Higher plasma omega-3 fatty acid status in the moderately healthy elderly in Southern Québec: higher fish intake or aging-related change in omega-3 fatty acid metabolism? Prostaglandins, Leukotrienes and Essential Fatty Acids, 82(4-6), 277-280.

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Pifferi, F., Jouin, M., Alessandri, J.-M., Roux, F., Perrière, N., Langelier, B., Lavialle, M., **Cunnane, S. C.**, & Guesnet, P. (2010). Omega-3 long-chain fatty acids and regulation of glucose transport in two models of rat brain endothelial cells. Neurochemistry International, 56(5), 703-710.

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Principal research support

1. University Research Chair: 'New neuroimaging methods to better understand brain aging' (2011-2018).
   Goal: To integrate multi-MRI and PET imaging to advance the understanding of brain fuel metabolism during aging.
2. Canadian Institute of Health Research: 'Brain fuel metabolism and risk of cognitive decline in the elderly' (2010-2015).
   Goal: To measure brain fuel uptake quantitatively using PET and MRI in healthy older versus young adults.
3. Natural Sciences and Engineering Research Council: 'Fatty acid and ketone metabolism during healthy aging' (2014-2019).
   Goal: To assess how plasma ketone response changes after nutritional and pharmaceutical interventions designed to induce mild nutritional ketonemia.
4. Alzheimer Association USA: Proof of concept of a ketogenic supplement in mild cognitive impairment. (2015-2017).
   Goal: To assess the impact of a ketogenic supplement on brain imaging outcomes in mild cognitive impairment.
5. Pfizer-FRQS (Quebec): Triheptanoin and intra-nasal insulin to correct the energy deficit in the aging brain (2015-2017).
   Goal: To assess whether triheptanoin +/- intra-nasal insulin can correct impaired glucose uptake in the frontal cortex of older people.