Tim Bartness (1953–2015)

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TIM BARTNESS died on September 24, 2015 at his home in Atlanta after a year-long battle with multiple myeloma. He was 62 years old. Tim was a superbly innovative and imaginative scientist. Over the course of his distinguished career he applied a broad understanding of metabolic physiology, behavior analysis, and systems neuroscience to two main research areas: the integrated sensorimotor control of adipose tissue function; and the neural bases of food hoarding behavior.

Tim obtained his PhD in Psychology and Neuroscience working with Robert Waldvillig at the University of Florida in 1981. Waldvillig had trained with Neal E. Miller, a true pioneer and leader in research on the neural basis of motivated behavior. Tim and Robert published 10 papers together on a range of topics that included effects of estradiol treatment on dietary self-selection, insulin on drinking, and serotonin depletion on food intake, locomotion, body weight, and adiposity. Tim went on to two postdocs, first at the University of Massachusetts (Amherst), followed by the University of Minnesota (Minneapolis). He then moved in 1984 to a more senior position at the Worcester Foundation For Experimental Biology in Shrewsbury in Massachusetts. In 1988 Tim moved from the Worcester Foundation to a junior faculty position in the Department of Psychology and later in Biology at Georgia State University (GSU) in Atlanta, which was to be his academic home for the remainder of his career (Fig. 1).

The breadth of science and scholarship he acquired in his postdoc years enabled Tim to develop the insight that it would not be possible to understand the full repertoire of feeding and metabolic control mechanisms by relying solely on rats and mice as experimental models. At the University of Massachusetts, his first postdoctoral mentor George Wade (who had trained with Irv Zucker at University of California, Berkeley; Tim and Irv were to become friends), had worked for some time with hamsters to investigate the neural control of metabolism. At first glance, a focus on the hamster might seem a strange choice given the preponderance of mice in current mammalian physiology and neuroscience. But working with Wade showed Tim that hamsters possess two very useful properties for understanding how the brain controls energy metabolism: the amount of adipose tissue carried by some hamster species is heavily influenced by the prevailing photoperiod and the circadian clock on the way that Siberian hamster (Phodopus sungorus) as a primary animal model for a considerable part of his research output. This decision allowed him to focus on important metabolic control mechanisms, particularly those residing in the brain, in a way that was not possible in rats and mice. His choice was a beautiful illustration of the fact that nature can provide you with the best models for studying physiological mechanisms, so long as you are intellectually prepared to choose them wisely. In the current environment where the strong desire for understanding genes and molecular mechanisms governing behavior drives so many experimental designs toward mouse models, Tim’s death is a significant loss. It means that the field has lost an effective advocate for alternate physiology-driven animal models.

Tim published a set of papers in the latter half of the 1980s with Allen Levine, Charles Billington, John Morley, and others at the University of Minnesota that addressed the role of various neuropeptides in energy homeostasis. This was followed by work with Bruce Goldman, Eric Bittman, and others at the Worcester Foundation that explored the influence of the photoperiod and the circadian clock on the way that Siberian hamsters control their body weight and adiposity as the day length changed. These extensive postdoc experiences gave Tim a solid and astutely structured foundation for establishing his own research program at GSU in 1988.

The first few years of Tim’s research at GSU were dedicated to expanding his previous work on photoperiodic influences on energy metabolism and particularly exploring the role of neuroendocrine factors and hormones. However, it quickly became apparent that a full understanding of how the brain controls adipose tissue physiology would only emerge from a more thorough neuroanatomical investigation of the sensory and
motor innervation of both white (WAT) and brown adipose tissues (BAT).

The fact that WAT is innervated by sympathetic motor fibers had been known since the mid-1960s. But whether this catecholaminergic innervation was related to lipolysis or to local vascular control was still unclear. To clarify this system Tim embarked on a highly successful venture to examine in great detail the structural and functional aspects of adipose tissue innervation; a topic that was still very active in his lab at the time of his death.

The first of many papers on this topic was published with Timothy Youngstrom in 1995 (13). It examined the role of the sympathetic nervous system in driving the effects of short day length on internal (epididymal) and external (inguinal) fat pads of Siberian hamsters. Tim Bartness had shown a few years earlier that internal fat pads were more responsive to photoperiod-induced changes than external fat pads. To determine whether the brain played a role in this phenomenon, they asked if these pads were innervated by catecholaminergic sympathetic motor neurons, and whether manipulating this innervation had differential effects on their lipolysis rates. Positive findings would support the idea that autonomic drive, and therefore control from the brain, was a significant factor for controlling WAT function. The study used fluorogold (FG), an efficient retrograde tracer that had been used widely for about 10 years, to identify afferent projections in the brain. It showed that FG-labeled neurons from injections into inguinal and epididymal fat pads were differentially distributed across T13-L3 sympathetic ganglia after FG. Collectively, these neurochemical and neuroanatomical findings provided a viable centrally controlled mechanism for mediating photoperiodic influences on WAT.

Although high-sensitivity neuroanatomical tracers such as FG are very effective at identifying neural pathways, they only identify the projections of single neurons. Because of the ability of neurotropic viruses to infect neurons trans-synaptically, the next generation of tracing methods used such agents, particularly the retrogradely transported variants of the pseudorabies virus (PRV), to reveal the deeper brain network that controlled the sympathetic innervation of adipose tissue. Tim and his colleagues made full use of this property to explore how the brain controls WAT and BAT function.

In a series of highly cited papers beginning in 1998, Tim worked with Kay Song, Maryam Bamshad, and others to apply PRV first to WAT (1), and then BAT (2), to show that many of their control neurons were located in the main autonomic control regions in the hindbrain and forebrain. These findings firmly established that the central autonomic control network can have a major influence on the sympathetic innervation of WAT and BAT. Tim also examined whether WAT received a significant parasympathetic innervation and concluded unambiguously that it did not (5). This result was the source of some controversy given the positive findings from others (6, 7). But the lack of additional corroborating evidence for parasympathetic innervation subsequently supported Tim’s original assertion (4).

The next phase of this research for Tim and his trainees was to use a variant of the herpes simplex virus H129 (HSV1 H129) to show the sensory innervation of WAT and BAT. In contrast to PRV, HSV1 H129 is transported anterogradely within infected neurons and therefore identifies in a sequential manner, those neurons that receive sensory information from WAT and BAT (11, 12). These results showed for the first time that the brain not only receives information about the current state of adipose tissue by way of circulating leptin, but also directly through sensory nerves that travel in the vagus nerve and spinal cord. A further element that Tim later added to this story is that WAT sensory nerves are also leptin sensitive (8), a finding that added further complexity to the crosstalk between these different sensory modalities. Taken together with the PRV findings showing that adipose tissue was innervated by sympathetic motor fibers, the implication from the HSV1 H129 experiments was that lipolysis in adipose tissue could be rapidly activated in response to appropriate sensory stimulation in a manner similar to the autonomic mechanisms controlling processes such as blood pressure. Also making important contributions to work from Tim’s lab on this topic area were Erin Keen-Rheinhardt, Michele Foster, Cheryl Vaughn, Yogendra Shrestha, Claudia Leitner, and Heifei Shi.

In the past few years Tim and his colleagues took a further step toward clarifying the structure of adipose tissue control networks in the spinal cord and brain. Working with Vitaly Ryu, Tim showed that individual neurons in the spinal cord and brain received sensory information and contributed to the networks that control sympathetic motor output to WAT. To do this they combined PRV and HSV1 H129 injections into WAT pads in Siberian hamsters. These dual injections generated double-labeled neurons in the spinal cord and further rostrally in the brain (9). Thus these particular neurons can act as key links for short (in the spinal cord) and long (deeper in the brain) WAT sensorimotor feedback loops. Tim had postulated the existence of these afferent-efferent control loops when he first identified the sensory innervation of WAT using HSV1 H129 (11). At the time of Tim’s death, he and Vitaly Ryu were further developing this concept by using the same virus coinjection technique to examine structural interactions between WAT and BAT control networks.

The role of the photoperiod and the neural control of adipose tissue function formed the bulk of Tim’s research. But it is also notable that he was one of the few that studied the neural bases of food hoarding behavior in hamsters. Going all the way back to his work with George Wade, Tim had maintained that there was great value to the field in studying this fundamental appetitive behavior. Recognizing the similarities with human responses (3), Tim worked with Diane Day, Brett Taubner, Megan Dailey, Johnny Garrettson, and others in his lab to explore the neuroendocrine bases of this behavior, particularly in the hypothalamus. As mentioned earlier, Tim’s premature death means that this important and fascinating topic has lost an key contributor.

At this juncture, it is worth noting that many of Tim’s key papers were published in the American Journal of Physiology, particularly its Regulatory, Integrative and Comparative Physiology Section. Tim had a long and very productive publishing relationship with this journal. Of the more than 180 papers that he published during his 35-year career, over a third of them were in this journal, including two of his most highly cited papers (1, 2).

Tim’s ability to identify and make compelling contributions to cutting-edge research topics had a clear and positive impact on how well and continually funded by the National Institutes of Health (NIH) he and his many students have been. His
primary R01 that National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) awarded to support his adipose tissue work was in its thirty-first year when he died. Notably, this grant was funded as a prestigious 10-year R37 merit award until 2019 when he died. Tim also held a R01 from NIDDK for his work on food hoarding that was in its second 5-year period. Many of his students were awarded F31 and F32 National Research Service Awards.

Tim contributed enormously to the academic environment at GSU where he was deeply involved with research programs, undergraduate and graduate teaching, and student mentoring. These efforts gained him many supporters and garnered him a number of awards. He was appointed Regents Professor at Georgia State in 2007 and was awarded the Georgia State University Faculty Award for Undergraduate Research in 2011. To help expand the obesity research at his home institution he was appointed Director of the GSU Center for Obesity Reversal in 2014. He was elected a Fellow of the American Association for the Advancement of Science (AAAS) in 2012.

Tim was a passionate advocate for his field. He targeted his efforts in three main directions: the Society for the Study of Ingestive Behavior (SSIB), where he served in a variety of positions including as its President in 2008–2009; The Obesity Society (TOS), where he served on their program committee; and service to the NIH Center for Scientific Review (CSR), where for many years he was an influential and committed reviewer, and an effective advocate on various study sections, most notably Neuroendocrinology, Neuroimmunology and Behavior (NNB, now NNRS) and more recently Integrative Physiology of Obesity and Diabetes (IPOD). Because he was what might be described as a systems level physiologist, Tim was often able to present an effective and considered counter-balance to the reductionism that has dominated the field of metabolic physiology and neuroscience for a number of years.

Working with SSIB, TOS, and other forums led to many deep and long-lasting friendships. These friendships mixed science, collegiality, socializing, and a deep love of music, notably classic rock, blues, and jazz. Over the years, he published papers with many of these friends including Charles Billington, Harvey Grill, Allen Levine, Gary Schwartz, and especially his long-time partner Ruth Harris.

Tim had passions for science, student mentoring, engaging his friends, and listening to and playing music. His comprehensive knowledge of metabolic physiology combined with keen appreciation for neural structure and function engendered a broad and valued perspective about how the brain and periphery interact to control energy metabolism, as well as their implications for dealing with obesity and its accompanying pathologies. Tim’s active and engaged presence is greatly missed by many.

REFERENCES


