Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

ELSEVIER

Physiology & Behavior 72 (2001) 721–726

PHYSIOLOGY & BEHAVIOR

Feeding behavior during sialodacryoadenitis viral infection in rats

Tomoi Sato[a], Michael M. Meguid[a,*], Robert H. Quinn[b], Lihua Zhang[a], Chung Chen[c]

[a]*Neuroscience Program, Surgical Metabolism and Nutrition Laboratory, Department of Surgery, SUNY, Upstate Medical University, University Hospital, 750 East Adams Street, Syracuse, NY 13210, USA*

[b]*Department of Laboratory Animal Resources, SUNY, Upstate Medical University, University Hospital, Syracuse, NY, USA*

[c]*Department of Quantitative Methods, Syracuse University, Syracuse, NY 13244-1150, USA*

Received 29 August 2000; received in revised form 7 December 2000; accepted 2 January 2001

Abstract

Sialodacryoadenitis (SDA) is a highly contagious common viral infection in rats, akin to mumps in humans. Anorexia occurs during such viral infection. But the pattern of the decrease in food intake (a decrease in either meal size and meal number or both) during spontaneous viral infection has not been previously characterized. We observed the onset of anorexia and an abnormal feeding pattern during an opportunistic SDA viral infection in our rat colony. We thus studied seven male rats. Before the viral infection there was a positive association between food intake and meal number ($P < .05$). After infection food intake decreased by 68%. This occurred via a significant decrease in meal size (by 69%) ($P < .05$); and a nonsignificant decrease in meal number ($P = .71$). This pattern of decreased food intake is similar to that occurring during indomethacin-induced ulcerative ileitis, where we previously measured an increase in plasma tumor-necrosis factor (TNF)-α. Anorexia in response to bacterial lipopolysaccharide administration, which is also linked to plasma TNF-α, is however, caused only via a decrease in meal number. The differences in the decrease in the feeding pattern between the SDA viral and a bacterial infection suggest that factors other than TNF-α alone play a significant role in the mechanism of anorexia during a viral infection.

Keywords: Sialodacryoadenitis; Food intake; Meal size; Meal number; Cytokines; Anorexia; Indomethacin-induced ulcerative ileitis

1. Introduction

Anorexia occurs during acute and chronic diseases. In an acute infectious disease, anorexia can be rationalized to provide some beneficial effect: metabolic switch to hepatic acute phase protein synthesis, rest of gastrointestinal tract or prevention of bacterial growth via reduced availability of nutrients essential for microorganisms [1], resulting in better prognosis [1]. In a chronic disease such as cancer, the chronicity of anorexia leads to malnutrition, body weight loss and eventually cachexia [2]. The mechanism(s) of anorexia is multifactorial and includes both peripheral and central factors [3], which await further identification.

Daily food intake (FI) is a function of meal size (MZ) and meal number (MN; FI*f*MZ × MN), which constitute feeding pattern. Under normal conditions, the constancy of daily food intake is maintained via a reciprocal change in meal size and meal number. This suggests that meal size and meal number be regulated independently via closely coordinated systems [4–6]. Under pathological conditions, a reduction of food intake occurs via a reduction of either meal size or meal number or both, thus providing insights into the etiology and the possible mechanisms of the pathogenesis of eating behavior [6]. An Automated Computerized Rat Eater Meter (ACREM; [7]), which measures individual meal size and meal number as well as food intake for prolonged periods, provides us with the ability to characterize the biological manifestations associated with feeding behavior including anorexia.

Sialodacryoadenitis (SDA) is a common short-lived acute infection in rats caused by a coronavirus, and is akin to mumps in humans. It is highly contagious among rats and spreads by the respiratory route [8]. SDA has a high morbidity but usually a low mortality with mild clinical signs: squinting, photophobia, blinking, sneezing, and/or

* Corresponding author. Tel.: +1-315-464-6277; fax: +1-315-464-6237.

E-mail addresses: meguidm@upstate.edu

0031-9384/01/$ – see front matter
PII: S0031-9384(01)00420-6

swelling under the neck caused by either edema, enlarged cervical lymph node, or inflamed salivary glands. Normally rats recover within 1 week [8]. Anorexia during an influenza virus-induced infection was previously documented [9–11], but the feeding pattern during a similar viral infection has not been previously reported.

An opportunistic SDA viral infection occurred in our male Fischer-344 rat colony and provided the spontaneous opportunity to measure and document changes in the feeding pattern with the ensuring anorexia. Our data provide further insight for understanding the mechanism(s) of anorexia and its associated changes in feeding pattern during an acute viral infection.

2. Materials and methods

2.1. Animals

Male Fischer-344 rats (Taconic, Georgetown, NY), with a purchase weight of 230 g, were housed in holding cages for 7 days to acclimate them to the constant study surroundings; 12-h light/dark cycle (lights on 0500–1700 h), 26 ± 1°C room temperature, and 45% relative humidity. Rats had free access to fresh coarsely ground chow (Diet #5008; RalstonPurina, St. Louis, MO) and tap water.

2.2. Feeding pattern measurement

When the outbreak of an SDA viral infection in the rat colony was first suspected, seven acclimated and apparently healthy rats were placed in the ACREM cages whose function was previously described in detail [7]. The ACREM continuously measures meal size, meal number, and food intake for a prolonged period, without preconditioning or pretraining the rats. Food access, via a feeding tunnel, is monitored via photocells. Food consumption is measured via an electronic scale. Both data are integrated in real-time and continuously recorded during successive light/dark cycles. A meal was defined as a bite or a series of bites preceded and followed by at least 5 min of feeding inactivity. Body weight was measured daily. The rats were studied until they appeared to have clinically recovered from the SDA viral infection.

2.3. Confirmation of the presence of virus infection

During 10 days of feeding pattern measurement, food intake dramatically decreased when the rats become clinically symptomatic. At the same time, three other rats (the same age and the same body weight) in the same colony room were randomly selected and were euthanized using carbon dioxide. Blood was immediately collected via cardiac puncture, and serum was obtained and stored in −20°C. Serologic testing (Charles River Lab, Wilmington, MA) was performed via enzyme-linked immunosorbent assay (ELISA) for the following viruses: SDA virus/rat coronavirus, Sendai virus, pneumonia virus of mice, Kilham rat virus, Toolan's H-1 virus, mouse polio virus, reovirus type 3, mycoplasma pulmonis, lymphocytic choriomeningitis virus, mouse adenovirus FL/K87, and rat parvovirus NS-1. In addition, because the specificity of ELISA is slightly low, immunofluorescent antibody testing was performed for the SDA virus. We also performed bedding contact surveillance to confirm the presence of the SDA viral infection in the colony.

2.4. Statistical analysis

Because the time at which initial infection occurred in each rat could not be detected, data were synchronized on the day (defined as Day 0) when their food intake decreased by 30% of their average daily food intake before clinical infection. Data are shown from Days −5 to 7 for body weight and from Days −4 to 6 for food intake, meal size, and meal number. Data of food intake, meal size, and meal number were analyzed via one-way ANOVA and as a post hoc test using paired t test between the average value and each value on each day. We calculated the correlation between food intake and meal size or food intake and meal number before and after infection using Pearson correlation coefficient to determine their association. The P value is calculated to test the null hypothesis that there is no correlation between food intake and meal size or food intake and meal number. Because body weight continuously increased from Days −5 to 0 and then started to decrease from Day 1, body weight after Day 1 was compared with that on Day 0 via paired t test. Data indicate mean ± standard error. A P value less than .05 was accepted as significant.

3. Results

3.1. Clinical sign and body weight

Enlarged lymph nodes were palpated in the neck in all rats. No rat died. As shown in Fig. 1, body weight from Days −5 to 0 continuously increased, but from Days 1 to 7, body weight was significantly decreased as compared with that on Day 0.

3.2. Food intake, meal size, and meal number

As shown in Fig. 2a, food intake was significantly decreased from Days −2 to 5. This decrease in food intake occurred primarily via a decrease in food intake during light phase, followed thereafter by a decrease in food intake during dark phase after Day 1. Food intake during light phase recovered faster than that during dark phase (data not shown). Food intake reached nadir on Day 1 (32.2 ± 11.8%

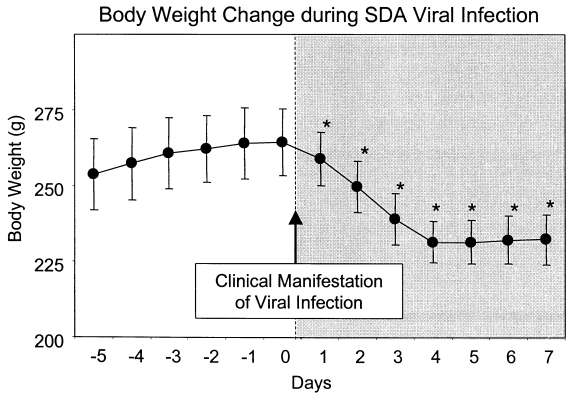

Fig. 1. Body weight change during the SDA viral infection. Asterisks (*) indicate a P value less than .05 vs. Day 0, which is defined as the day of clinical manifestation of the viral infection.

relative to baseline). Finally, food intake returned to the average value on Day 6. Before the viral infection, there was a positive association between food intake and meal number ($P < .05$). As shown in Fig. 2b, meal size started to decrease on Day 0, and significantly decreased from Days 1 to 4. After infection, food intake decreased by 68%. This occurred via a significant decrease in meal size ($P < .05$), while meal number decreased nonsignificantly ($P = .71$).

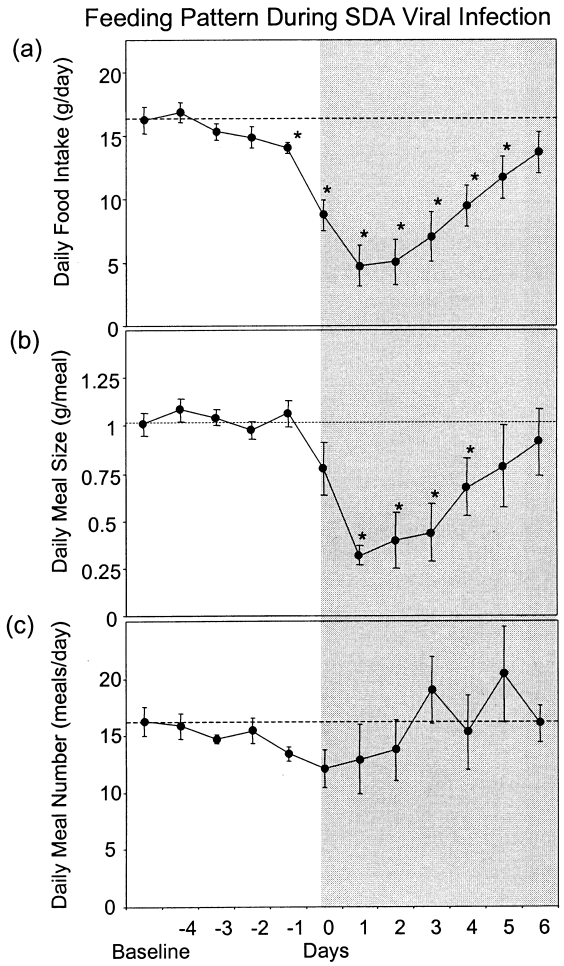

Fig. 2. Daily food intake, meal size, and meal number before and during the SDA viral infection. Dotted lines indicate baseline. Asterisks (*) indicate a P value less than .05 vs. baseline.

Table 1
Result of serologic testing of rats

Method	Agent	Rat #1	Rat #2	Rat #3
ELISA	SDA/RCV	+	+	+
IFA	SDA/RCV	+	+	+
ELISA	SEND	–	–	–
ELISA	PVN	–	–	–
ELISA	KRV	–	–	–
ELISA	H-1	–	–	–
ELISA	GD-7	–	–	–
ELISA	REO-3	–	–	–
ELISA	MPUL	–	–	–
ELISA	LCMV	–	–	–
ELISA	MAD	–	–	–
ELISA	RPV NS1	–	–	–

ELISA: enzyme-linked immunosorbent assay; IFA: immunofluorescent antibody; SDA/RCA: sialodacryoadenitis virus/rat coronavirus; SEND: Sendai Virus; PVM: pneumonia virus of mice; KRV: Kilham rat virus; H-1: Toolan's H-1 Virus; GD-7: mouse polio virus; REO-3: reovirus type 3; MPUL: mycoplasma pulmonis; LCMV: lymphocytic choriomeningitis virus; MAD: mouse adenovirus FL/K87; RPV NS1: rat parvovirus NS-1.

Similarly to food intake data, meal size reached nadir on Day 1 ($31.5 \pm 5.2\%$ relative to baseline). There was no difference in meal size findings between the light and dark phases. As shown in Fig. 2c, meal number from Days -4 to 6 did not significantly decrease. The maximum decrease in meal number occurred on Day 0 ($78.0 \pm 13.8\%$ relative to baseline; $P = .06$). Meal number during light phase on Days -2 and -1 decreased significantly, but it was offset by an increase in meal number during dark phase. During recovery, meal number slightly increased predominantly via an increase in meal number during light phase (data not shown).

3.3. The presence of SDA virus

Bedding contact surveillance of rats showed positive results for the SDA virus. As summarized in Table 1, serologic testing also showed positive results only for the SDA virus both in ELISA and immunofluorescent antibody testing and showed negative results for all the other viruses. After confirmation of the presence of the SDA viral infection, all rats in our colony were euthanized using carbon dioxide.

4. Discussion

Although we measured serologic testing in only three rats in the same colony, the highly contagious nature of the SDA virus and the fact that all rats eventually developed

symptoms and signs of infection left little doubt that all rats in our colony ($n = 62$), including those in the ACREM, developed the viral infection.

To our knowledge, these data presented here are the first demonstration of abnormal feeding patterns during an SDA viral infection. Our data showed that anorexia during the SDA viral infection occurred predominantly via a decrease in meal size. Meal number did not decrease significantly, and did not simultaneously increase in a compensatory manner, in an attempt to maintain constancy of food intake, so consequently, food intake decreased, which was associated with body weight loss.

An approximation of the amount of weight loss due to the decreased food intake can be determined based on the following calculations in which the metabolizable energy of the food is 3.31 kcal/g (Purina Formulab Diet #5008). The average decrease in food intake per rat was about 6.4 g/day. This calculates to an average decrease of 21.2 kcal/day/rat. For maintenance, a rat needs approximately 110 kcal/kg$^{0.75}$/day [12], which corresponds to 40.6 kcal/day for the average rat in this study which weighed 265 g. The rats started out eating an average of 17 g/day, which equals 37.3 kcal/day. The difference is probably attributable to errors inherent in averaging both the animal weights and food intake. Over the 10-day period of decreased intake, this was reduced by 21.2 kcal/day to an average intake of 16 kcal/day. Since they require about 40 kcal/day and they were taking in 16 kcal/day, there was a net loss of 24 kcal/day. Conversion of protein, fats, and carbohydrates produces an average gain of approximately 6.4 kcal/g [13]. This roughly corresponds to an average weight loss of about 3.75 g/day or 37.5 g/rat over the 10-day period of decreased intake. It appears that the average rat lost approximately 30 g; the difference being attributable to averaging variable of animals, imprecision in the calculations, and other factors that make this only an estimation. It would appear that the entire loss of body weight could be accounted for by the decrease in food intake, although other unmeasured factors (such as changes in metabolic requirements) were not examined.

Furthermore, there was a difference in the pattern of the decrease and the recovery in food intake and meal number between light and dark phases. The different pattern in the dynamics of meal size and meal number suggests that meal size and meal number be regulated independently via different systems [6].

This pattern of food intake decrease is different from that which occurs during the anorexia of bacterial lipopolysaccharide (LPS)-induced infections [14–16] or in cancer [17]. But, it is similar to that of anorexia of indomethacin-induced ulcerative ileitis, where we previously measured an increase in plasma tumor-necrosis factor (TNF)-α [18]. The SDA virus belongs to the coronavirus family, which has been documented to increase TNF-α [19]. Pentoxifylline (an anti-TNF-α agent) inhibits TNF-α induced hypophagia [20]. It is interesting to note that with recovery from the SDA viral infection, meal number slightly increased. This pattern of recovery may represent the process of normalization of food intake during the recovery period after human viral infection, such as mumps or influenza.

During an SDA viral infection, inflamed salivary glands and/or swollen neck lymph nodes occur. Hence, the observed decrease in meal size could be influenced via mechanical obstruction or diminished salivary secretion. However, under normal conditions, a decrease in either meal size and meal number is offset by an increase in the other to maintain the constancy of daily food intake. Thus, the lack of a compensatory increase in meal number during the SDA viral infection might indicate abnormal and impaired feeding behavior.

In anorexia of acute and chronic diseases, various cytokines [e.g., TNF-α, interleukin (IL)-1, IL-2, IL-6, IL-8, interferon (IFN), etc.] alone or synergistically play a significant role [3,21,22]. During bacterial and viral infections, microbial products such as bacterial cell wall compounds [e.g., LPS and muramyl dipeptide (MDP)], microbial nuclei acids (e.g., bacterial DNA and viral double-stranded RNA) and viral glycoproteins stimulate the host's acute phase response [14,15,23–25]. These cytokines act directly or indirectly on the hypothalamus [21,26,27].

Previously we reported that in food-deprived rats, changes in dopamine concentration in the lateral hypothalamic area (LHA) positively correlated with changes in meal size [28,29], while those in the ventromedial nucleus in the hypothalamus (VMN) negatively corresponded to intermeal interval, and thus influenced meal number [30,31]. In the septic rat model, induced by cecal ligation and puncture, dopamine concentration in the VMN progressively decreased and this reduction of dopamine concentration was associated with anorexia [27]. Hence, cytokines, induced by microbial products, may influence anorexia and feeding patterns via changes in the concentration of hypothalamic dopamine [32], among other neuromediators.

Anorexia, both induced by peripheral IL-1α injection and in methylcholanthrene-induced sarcoma-bearing male Fischer-344 rats, was produced by predominantly an initial decrease in meal number, followed a day later by a decrease in meal size [17,33]. While anorexia, induced by LPS or MDP, derived from the cell wall of gram-negative or -positive bacteria, respectively, was produced by only a decrease in meal number; meal size was not affected [14–16]. The mechanisms of anorexia induced by these bacterial products are similar [14,15], and TNF-α has been repeatedly shown to play a significant role in the mechanisms of anorexia during bacterial infection [10,16].

It appears that gender differences exist in the acute phase response [34]. Previously, we reported that in female Lewis rats with indomethacin-induced ulcerative ileitis, food intake decreased mainly via a decrease in meal size and to a lesser extent via a decrease in meal number [18]. This decrease in meal size correlated negatively with plasma TNF-α [18]. Even when considering difference in gender and rat strain, the changes in food intake and feeding pattern

between the SDA viral infection and the indomethacin-induced ulcerative ileitis model is similar. These changes have not been previously observed in the other rat models in both genders (e.g., in MCA sarcoma-bearing female Fischer-344 rat model, food intake decreases only via a decrease in meal number; [35]). Thus, the similarity in pattern of decreased food intake during the SDA viral infection and that during indomethacin-induced ulcerative ileitis, suggests a mechanistic link between viral infection, TNF-α, and anorexia. Furthermore, data that an infection with the influenza virus is associated with increased TNF-α activity in lung lavage fluid of male Swiss–Webster mice [11], and the manifestation of severe anorexia even in IL-1β-deficient mice [10], suggest a significant and limited role of TNF-α and IL-1β in anorexia during a viral infection, respectively.

Although the mechanism of anorexia during bacterial and viral infection is linked to TNF-α, the difference in feeding pattern between the SDA viral infection and a bacterial infection suggests involvement of factors, other than TNF-α and IL-1β during these infections. Thus, during an SDA virus infection, additional cytokines, such as IL-2, IL-6, IL-8, and/or IFN, may play a contributory role in decreasing food intake [3,11]. Particularly, a recent study suggests a role for IFN-γ in causing hypophagia and hypermetabolism during infection [36]. Since these cytokines act on the hypothalamus to modulate food intake and feeding behavior, they might have a direct or an indirect influence on the LHA to decrease meal size and on the VMN to inhibit a compensatory increase in meal number during the SDA virus infection.

References

[1] Murray MJ, Murray AB. Anorexia of infection as a mechanism of host defense. Am J Clin Nutr 1979;32:593–6.

[2] Langstein HN, Norton JA. Mechanisms of cancer cachexia. Hematol Oncol Clin North Am 1991;5:103–23.

[3] Plata-Salaman CR. Anorexia during acute and chronic disease. Nutrition 1996;12:69–78.

[4] Becker EE, Kissileff HR. Inhibitory controls of feeding by the ventromedial hypothalamus. Am J Physiol 1974;226:383–96.

[5] Levitsky DA. Feeding patterns of rats in response to fasts and changes in environmental conditions. Physiol Behav 1970;5:291–300.

[6] Meguid MM, Laviano A, Rossi Fanelli F. Food intake equals meal size times meal number. Appetite 1998;31:404.

[7] Meguid MM, Kawashima Y, Campos ACL, Gelling PD, Hill TW, Chen TY, Yang ZJ, Hitch DC, Hammond WG, Mueller WJ. Automated computerized rat eater meter: description and application. Physiol Behav 1990;48:759–63.

[8] Harkness JE, Wagner JE. Sialodacryoadenitis. The biology and medicine of rabbits and rodents. 3rd ed. Philadelphia: Lea & Febiger, 1989. pp. 186–8.

[9] Klein MS, Conn CA, Kluger MJ. Behavioral thermoregulation in mice inoculated with influenza virus. Physiol Behav 1992;52:1133–9.

[10] Kozak W, Zheng H, Conn CA, Soszynski D, Van Der Ploeg LHT, Kluger M. Thermal and behavioral effects of lipopolysaccharide and influenza in interleukin-1β-deficient mice. Am J Physiol 1995;269: R969–77.

[11] Conn CA, McClellan JL, Maassab HF, Smitka CW, Majde JA, Kluger MJ. Cytokines and the acute phase response to influenza virus in mice. Am J Physiol 1995;268:R78–84.

[12] Rogers AE. Nutrition. In: Baker HJ, Lindsey JR, Weisbroth SH, editors. The laboratory rat, vol. 1. Biology and diseases. New York: Academic Press, 1979. p. 128.

[13] Lewis LD, Morris ML, Hand MS. Nutrients. In: Lewis LD, Morris ML, Hand MS, editors. Small animal clinical nutrition III. Topeka, KS: Mark Morris Associates, 1987. pp. 1–7.

[14] Langhans W, Harlacher R, Balkowski G, Scharrer E. Comparison of the effects of bacterial lipopolysaccharide and muramyl dipeptide on food intake. Physiol Behav 1990;47:805–13.

[15] Langhans W, Balkowski G, Savoldelli D. Differential feeding responses to bacterial lipopolysaccharide and muramyl dipeptide. Am J Physiol 1991;261:R659–64.

[16] Porter MH, Arnold M, Langhans W. TNF-α tolerance blocks LPS-induced hypophagia but LPS tolerance fails to prevent TNF-α-induced hypophagia. Am J Physiol 1998;274:R741–5.

[17] Meguid MM, Sato T, Torelli GF, Laviano A, Rossi-Fanelli F. An analysis of temporal changes in meal number and meal size at onset of anorexia in tumor-bearing male rats. Nutrition 2000;16:305–6.

[18] Veerabagu MP, Opara EI, Meguid MM, Nandi J, Oler A, Holtzapple PG, Levine RA. Mode of food intake reduction in Lewis rats with indomethacin-induced ulcerative colitis. Physiol Behav 1996;60:381–7.

[19] Itoh T, Iwai H, Ueda K. Comparative lung pathology of inbred strain of mice resistant and susceptible to Sendai virus infection. J Vet Med Sci 1991;53:275–9.

[20] Porter MH, Hrupka BJ, Altreuther G, Arnold M, Langhans W. Inhibition of TNF-alpha production contributes to the attenuation of LPS-induced hypophagia by pentoxifylline. Am J Physiol: Regul, Integr Comp Physiol 2000;279:R2113–20.

[21] Plata-Salaman CR, Oomura Y, Kai Y. Tumor necrosis factor and interleukin-1 beta: suppression of food intake by direct action in the central nervous system. Brain Res 1988;448:106–14.

[22] Yang ZJ, Koseki M, Meguid MM, Gleason JR, Debonis D. Synergistic effect of rhTNF-α and irIL-1α in inducing anorexia in rats. Am J Physiol 1994;267:R1056–64.

[23] Sparwasser T, Miethke T, Lipford G, Borschert K, Hacker H, Heeg K, Wagner H. Bacterial DNA causes septic shock. Nature 1997;386: 336–7.

[24] Majde JA, Guha TN, Chen Z, Bredow S, Krueger JM. Spontaneous release of stable viral double-stranded RNA into the extracellular medium by influenza virus-infected MDCK epithelial cells: implications for the viral acute phase response. Arch Virol 1998;143:2371–80.

[25] Ankel H, Westra DF, Welling WS, Lebon P. Induction of interferon-alpha by glycoprotein D of herpes simplex virus: a possible role of chemokine receptors. Virology 1998;251:317–26.

[26] Opara EI, Laviano A, Meguid MM, Yang ZJ. Correlation between food intake and CSF IL-1α in anorectic tumor bearing rats. NeuroReport 1995;6:750–2.

[27] Torelli GF, Meguid MM, Miyata G, Fetissov SO, Carter JL, Kim HJ, Muscaritoli M, Rossi Fanelli F. VMN hypothalamic dopamine and serotonin in anorectic septic rats. Shock 2000;13:204–8.

[28] Meguid MM, Yang ZJ, Koseki M. Eating induced rise in LHA-dopamine correlates with meal size in normal and bulbectomized rats. Brain Res Bull 1995;36:487–90.

[29] Yang ZJ, Koseki M, Meguid MM, Laviano A. Eating-related increase of dopamine concentration in the LHA with oronasal stimulation. Am J Physiol 1996;270:R315–8.

[30] Meguid MM, Yang ZJ, Laviano A. Meal size and number: relationship to dopamine levels in the ventromedial hypothalamic nucleus. Am J Physiol 1997;272:R1925–30.

[31] Yang ZJ, Meguid MM, Oler A. Eating-associated VMN-dopamine levels of rats: comparison of oral and intragastric feeding. NeuroReport 1997;8:1543–7.

[32] Yang ZJ, Blaha V, Meguid MM, Oler A, Zadak Z. Interleukin-1α injection into ventromedial hypothalamic nucleus of normal rats de-

presses food intake and increases release of dopamine and serotonin. Pharmacol, Biochem Behav 1999;62:61–5.

[33] Debonis D, Meguid MM, Laviano A, Yang Z-J, Gleason JR. Temporal changes in meal number and meal size relationship in response to rh-IL-1α. NeuroReport 1995;6:1752–6.

[34] Spitzer JA, Zhang P. Gender differences in neutrophil function and cytokine-induced neutrophil chemoattractant generation in endotoxic rats. Inflammation 1996;20:485–98.

[35] Chai JK, Varma M, Meguid MM, Torelli GF, Yang ZJ. Estradiol modulates tumor-induced anorexia and feeding pattern. Surg Forum 1998;XLIX:479–80.

[36] Arsenijevic D, Richard D. A predominant role for IFN-γ in infection induced cachexia in comparison to TNF-α (abstract)Appetite 1999; 33:232.