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Véronique V. Gayrard-Troy, Nicole Picard-Hagen, Catherine Viguié, Carole Delavaud, Pierre-Louis Toutain, Yves Y. Chilliard, . British Society of Animal Science

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V. Gayrard[1], N. Picard-Hagen[1], C. Viguié[1], C. Delavaud[2], P.L. Toutain[1] and Y. Chilliard[2]
[1]UMR INRA de Physiopathologie et Toxicologie Expérimentales, Ecole Nationale Vétérinaire de Toulouse, 31076 Toulouse, France et [2]Unité de Recherche sur les Herbivores, INRA Theix, 63122 St Genès-Champanelle, France

Introduction Scrapie is an ovine sub-acute transmissible spongiform encephalopathy (TSE) caused by unconventional transmissible agents. In several species, TSE are associated to major endocrinopathy, such as hyperinsulinemia and hypercorticism (Carp *et al*, 1990, Gayrard *et al*, 2000). Cachexia is commonly observed in the clinical phase of the prion disease. Our objective was to investigate if scrapie is associated to alterations of GH axis, leptin, insulin and metabolic parameters. In addition, central adrenergic system being affected in TSE (Braun *et al*, 1999), we investigated a possible alteration of α2-adrenergic control of GH axis associated to the prion disease.

Materials and methods Blood samples were collected every 30 min to determine the 24-h spontaneous pattern of GH plasma concentrations. GH response to intravenous administration of xylazine, an alpha2-agonist (0.15mg/kg) was determined in seven control and seven scrapie-affected ewes. For other determinations blood, samples were obtained before and 3 hours after morning meal. The ewes were tied in metabolism cages and received hay *ad lib* and two meals of 260 g of concentrates daily. Feed intake was not modified by the disease. The scrapie diagnosis was performed by histopathology. Body weights (mean ± SD) were 37±4 kg and 40±5 kg for scrapie-affected and control ewes, respectively. Plasma biochemical parameters and leptin were assayed by enzymatic methods or radioimmunoassay, respectively (Ferlay & Chilliard, 1999, Delavaud *et al*, 2000). In a separate period, in addition to plasma leptin concentrations, we assayed leptin in CSF sampled through a cannula inserted into a lateral ventricle. The influence of the disease and of meal on hormone and metabolite concentrations was assessed using ANOVA.

Results Plasma GH concentrations of scrapie-affected ewes tended to be greater than those observed in healthy ewes (mean±SD, 27.6±14.7 versus 16.8±12.6ng/ml), but the difference was not significant (P>0.1). Xylazine induced a transient and low increase in GH concentrations, with large interindividual variations. Mean plasma concentrations of some metabolites are given in Table 1. Plasma glucose and urea concentrations of scrapie-affected ewes were greater than those observed in healthy ewes (P≤0.05 and P=0.07 respectively). Mean insulin concentrations from diseased ewes were 2 fold higher compared with that of healthy ewes (P=0.07), whereas plasma IGF-1, leptin and 3-OH-butyrate concentrations were not affected by the prion disease. Post-prandial plasma NEFA concentration was lower in diseased ewes (P<0.05). CSF leptin concentrations were related to plasma leptin (r=+0.87; P<0.05) and unaffected by the prion disease (mean±SD, 1.6±0.9 and 1.3±0.4 ng/ml in 3 scrapie affected ewes and in 5 control ewes, respectively).

Table 1 Plasma concentrations (mean±SD) of IGF-1, leptin, insulin, glucose, NEFA, 3-OH-butyrate and urea in 7 scrapie-affected ewes and in 7 control ewes, sampled before and 3 hours after morning meal

	scrapie		control		Effect of scrapie
	before	after	before	after	P≤
IGF-1 (ng/ml)	133±61	ND	101±51	ND	NS
leptin (ng/ml)	3.7±0.31	3.6±0.27	4.3±1.1	4.2±0,9	NS
Insulin (µUI/ml)	24±13	28±19	11±3	15±7	0.07
Glucose (g/L)	0.74±0.1	0.74±0.08	0.58±0.06	0.57±0.07	0.005
NEFA (mmol/l)	0.36±0.19	0.13±0.07	0.29±0.19	0.30±0.28	NS [1]
3-OH-butyrate (mmol/l)	0.34±0.11	0.41±0.09	0.42±0.24	0.43±0.17	NS
Urea (g/l)	0.32±0.06	0.33±0.06	0.23±0.11	0.24±0.11	0.07

[1] Interaction meal*disease (P< 0.005) ND : not determined

Conclusions Collectively, these results suggest that scrapie does not change plasma nor CSF leptin concentrations but induces different hormonal and metabolic disorders, in particular, hyperinsulinemia, hyperglycemia, hyperuremia and a trend to higher GH secretion. The increase of urea concentrations could be related to myolysis or to renal disturbance. Hyperglycemia and hyperinsulinemia could be a consequence of the major hypercorticism shown in scrapie affected ewes (Gayrard *et al*, 2000) and could reflect a syndrom of resistance to insulin.

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