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# 1 **Hemodialysis affects *wanting* and spontaneous intake of protein-rich** 2 **foods in chronic kidney disease patients**

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50

51 **Running head:** *Wanting* and intake of protein after hemodialysis.

52

53 **Abbreviations:** AA, amino acid; CKD, chronic kidney disease; HD patients, hemodialysis  
54 patients; nPCR, normalized Protein Catabolic Rate; PEW, protein energy wasting; TFEQ, three-  
55 factor eating questionnaire.

56

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58

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62

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70

# 1 Hemodialysis affects *wanting* and spontaneous intake of protein-rich 2 foods in chronic kidney disease patients

## 3 ABSTRACT

4 **Background:** Protein-energy wasting is a risk factor for mortality and morbidity in  
5 hemodialysis patients (HD patients). Food intake could be modified by hemodialysis-related  
6 changes in the food reward system (*i.e.*, *liking* and *wanting* of specific macronutrients). In HD  
7 patients on days with and without dialysis, we evaluated: 1) the reward system for protein-,  
8 fat- and carbohydrate-rich foods, plasma hormones and metabolite changes; 2) the  
9 spontaneous *ad libitum* intake of macronutrients.

10 **Methods:** Twenty-four HD patients evaluated their *liking* and *wanting* of macronutrients at  
11 7:30 am and 11:30 am on a day with and a day without dialysis. Concentrations of hormones  
12 and plasma amino acids were determined. An additional 18 HD patients ate what they wanted  
13 from a buffet lunch comprising eight dishes on a day with and a day without dialysis. Healthy  
14 subjects, age-, sex- and BMI-matched, served as controls.

15 **Results:** At 11:30 am, *wanting* for protein-rich foods was higher on the day with than on the  
16 day without dialysis ( $P<0.01$ ), bringing *wanting* levels close to those of healthy subjects. This  
17 increase correlated with changes in the concentrations of plasma amino acids ( $P<0.01$ ). HD  
18 patients ate more protein from the buffet on the day with than on the day without dialysis  
19 ( $P<0.01$ ) and more than healthy subjects ( $P<0.01$ ).

20 **Conclusions:** In HD patients, *wanting* and spontaneous intake of protein-rich foods increase  
21 immediately after dialysis. This increase correlated with decreased concentrations of plasma  
22 amino acids. Thus, in clinical practice, protein-rich foods should be recommended during and after  
23 dialysis in patients with protein-energy wasting.

24

25 **Keywords:** Reward system, food intake, feeding behavior, chronic kidney disease, haemodialysis

26

27 **Abbreviations:** AA, amino acid; CKD, chronic kidney disease; HD patients, hemodialysis

28 patients; nPCR, normalized Protein Catabolic Rate; PEW, protein energy wasting; TFEQ, three-

29 factor eating questionnaire.

30

31

## 32 INTRODUCTION

33 Hemodialysis patients (HD patients) have a high risk of malnutrition and protein  
34 energy wasting (PEW) (1). Around 30-50% of chronic kidney disease (CKD) patients suffer  
35 from PEW and approximately 10% of patients on chronic dialysis show signs of severe PEW  
36 (2, 3). PEW increases the risk of cardiovascular complications, infection and death (4-6).  
37 Many factors are responsible for malnutrition in HD patients (7-9). Possible causes of  
38 malnutrition include difficulty absorbing certain macronutrients and needing to regulate the  
39 intake of salt and the consumption of certain minerals and liquids. There are also issues with  
40 vitamin supplementation, irregular food intake, the dialysis procedure itself, gastrointestinal  
41 upset and changes in the organs involved in nutrient metabolism, variations in the levels of  
42 some appetite-regulating factors (*e.g.*, leptin), depression, anorexia, comorbidities, and the  
43 conditions that lead to CKD themselves. Alterations in taste and smell (7, 10) also contribute  
44 to the development of malnutrition.

45 Food intake is controlled by complex interactions between homeostatic, cognitive, and  
46 hedonic processes (11-13). Homeostatic processes induce feelings of hunger or satiety (14),  
47 and are mainly related to metabolic and neuroendocrine factors (12, 15). Cognitive control  
48 comprises self-control, imposed regimen, socioeconomic and cultural influences,  
49 environmental and emotional factors, and beliefs about food (11). Finally, hedonic control  
50 relies mainly on the reward system (16) which comprises three main components: “*liking*”  
51 (pleasure/palatability); “*wanting*” (appetite/incentive motivation); and “*learning*”  
52 (preference/aversion), which is produced by associative conditioning and cognitive processes  
53 (17, 18).

54 It is accepted that HD patients often experience decreased hunger (*i.e.*, impaired  
55 homeostatic control of food intake) (19-22) and that the cognitive control of food intake is  
56 significantly affected by stringent medical constraints (23, 24). It is also common knowledge

57 that patients undergoing hemodialysis experience changes in food preferences, mainly in  
58 favour of sweet and salty foods, red meat refusal, and marked attraction to sour and strong  
59 flavors in general (25-27). However, to our knowledge, *liking* and *wanting* for the three types  
60 of macronutrients have never been studied in HD patients.

61 We therefore investigated the influence of hemodialysis on the hedonic control of food  
62 intake. In the first experiment, hunger, *liking* and *wanting* for the three macronutrients were  
63 evaluated before and after a normal scheduled session of hemodialysis. At the same time,  
64 plasma concentrations of hormones and amino acids (AAs) were measured. In the second  
65 experiment, spontaneous food choices and consumption of the three macronutrients were  
66 evaluated during a buffet lunch served after the hemodialysis. In both experiments, the same  
67 parameters were also measured in the same patients on a day without dialysis and in healthy  
68 subjects.

69

## 70 **SUBJECTS AND METHODS**

71 In EXP1, hunger, *liking* and *wanting* for the three macronutrients were evaluated in 24  
72 HD patients before (7:00-8:00 am) and after (11:00 am-12:00 pm) their dialysis, and at the  
73 same times on a day without dialysis. These items were also evaluated in 24 healthy subjects  
74 matched for sex, age and body mass index (BMI). Blood samples were drawn from HD  
75 patients immediately before and after dialysis and at the same times, in healthy subjects.

76 In EXP2, the spontaneous choices and consumption of eight nutritionally varied dishes  
77 from a buffet lunch were evaluated in 18 others HD patients on a day with and a day without  
78 dialysis. Results were compared with those of 18-matched healthy subjects evaluated using  
79 the same protocol for two successive days.

80 HD patients had 3-morning dialysis sessions per week. In both experiments, the day of  
81 dialysis was randomly drawn within the week. HD patients (aged 18 to 80 years) had to be



82 clinically stable for the previous preceding month. Healthy subjects had to have normal  
83 creatinine clearance ( $>60$  mL/min). Exclusion criteria were diabetes, malnutrition (BMI $<17.5$   
84 kg/m<sup>2</sup>, transthyretin $<0.25$  g/L), congestive heart failure, acute or chronic infection, ongoing  
85 antibiotic treatment, active cancer or liver cirrhosis, smoking ( $>5$  cigarettes/day), alcohol  
86 consumption ( $>3$  units of alcohol/day), oral nutritional supplements, aversions to the foods  
87 used in the study.

88 For HD patients, additional data were recorded: type of kidney disease, length of  
89 hemodialysis treatment, type of dialysis membrane, persistence of residual diuresis, adequacy  
90 of the dialysis according to the KT/V (28), body weight 3 and 6 months prior the study,  
91 normalized Protein Catabolic Rate (nPCR) (28), medical history and adjuvant treatments.

92

### 93 *EXPI*

#### 94 *Study design*

95 Before the experimental sessions, each participant completed the Three-Factor Eating  
96 Questionnaire (TFEQ) (29) to assess their food-related behavior. The TFEQ is a 51-item auto-  
97 questionnaire, which assesses three factors: the cognitive dietary restraint (conscious control  
98 of food intake with concerns about body shape and weight); the disinhibition of control  
99 (overconsumption of food due to a variety of stimuli associated with a loss of control over  
100 food intake); and the susceptibility to hunger (food intake or eating in response to feelings and  
101 subjective perceptions of hunger). All participants also completed a 3-day food eating  
102 questionnaire by recording all foods and beverages consumed during 3 days (one dialysis day,  
103 one day without dialysis and one weekend day), using household measures (a bowl, cup,  
104 glass, etc) to aid in portion size estimation.

105 On the morning of the sessions, HD patients and healthy subjects had to have their  
106 habitual breakfast (same composition and quantity before each session) at  $\sim 6:00$  am (*i.e.*  $\sim 1.5$

107 hours before the experimental measurements). Afterwards, participants could not eat until the  
108 end of the measurements. At ~7:30 am, in a neutral and calm environment, participants rated  
109 their hunger and evaluated their *liking* for six foods. The first two foods were rich in protein  
110 [Bündnerfleisch (dried beef) and imitation crab me], the next two were rich fat (melted butter  
111 and mayonnaise) and the last two were rich in carbohydrates (honey and strawberry jam).  
112 There were also two nonfood items (dishwashing liquid and toothpaste) used as controls.  
113 Each food and nonfood item were presented at random in separate small cups and smelled  
114 orthonasally for approximately 5-10 sec at a distance of 5-10 cm from the nose. Then,  
115 *wanting* for 18 other foods, presented as pictures showing typical protein-, fat- and  
116 carbohydrate-rich foods, was evaluated. The pictures showed, 1) a fried egg, grilled salmon,  
117 baked chicken, veal steak, rib steak, and turkey breast, 2) an avocado, olives, peanuts,  
118 chocolate, a doughnut, and whipped cream, 3) potato puree, rice, lentils, an apple, pasta, fruit  
119 cake. The pictures were presented separately for 10-15 sec in a random order. At ~11:30 am,  
120 participants rated again their hunger, *liking* and *wanting* using the same protocol. BMI was  
121 then evaluated and a dietician checked the 3-day dietary survey. During the interview, portion  
122 sizes were verified using the su.vi.max photos (30). Energy content and macronutrients  
123 composition of the ingested foods and beverages, were estimated using the nutrient software  
124 program Nutrilog Nutrition Software (Nutrilog SAS, France, 2016).

125

### 126 ***Subjective measurements***

127 Participants indicated their hunger sensation on 10-cm visual analog scale (VAS)  
128 anchored at its ends by the statements "not at all hungry" and "very hungry". They also  
129 indicated on 10-cm VASs their *liking* and *wanting* with the following questions, respectively:  
130 "How much do you like the odor of this food now?", "How much do you want to eat this food  
131 now?"

132

133 ***Blood parameters***

134 Hemoglobin and plasma sodium, potassium, calcium, phosphorus, albumin,  
135 transthyretin (biomarker of PEW in HD patients), protein, blood urea nitrogen, creatinine, C-  
136 reactive protein, ghrelin (hunger hormone), leptin (satiety hormone), insulin, and AAs were  
137 determined. Plasmatic concentrations of ghrelin and leptin were measured with ELISA kits  
138 (Millipore, Billerica, USA for ghrelin; R&D systems, Abingdon, UK for leptin). Insulin levels  
139 were determined by chemiluminescent immunoassay (Immulite 2000 WPi, Siemens  
140 Healthcare GmbH, Erlangen, Germany). Plasma AA concentrations were evaluated after  
141 deproteinization with sulfosalicylic acid (Sigma-Aldrich, Saint Quentin Fallavier, France) by  
142 ion-exchange chromatography (Hitachi High-Speed Amino Acid Analyzer L-8900, Hitachi  
143 High-Technologies Corporation, Tokyo, Japan) as previously reported (31). In HD patients,  
144 parathyroid hormone, transferrin saturation and total plasma CO<sub>2</sub> were also measured.

145

146 ***EXP2***147 ***Study design***

148 On the morning of the sessions, HD patients and healthy subjects were in the same  
149 feeding conditions as in EXP1. At ~12:30 pm (i.e. around their usual lunchtime), all  
150 participants rated their hunger and then evaluated their *liking* for eight dishes prepared by a  
151 caterer (see Supplemental Material 1) presented together on a tray. Each dish was smelled  
152 orthonasally then, each subject could choose the order and the quantities of each dish he  
153 wanted to eat. No time limit was imposed. The participants were not informed of the  
154 objectives of the study or that their intakes were precisely weighed. The entire meal contained  
155 7417 kJ (1773 kcal) with 23% of energy from protein, 65% from fat and 12% from  
156 carbohydrates. At the end of the meal, hunger and *liking* were evaluated again for the eight

157 dishes, and seven questions were added to evaluate how pleasant the meal was and the  
158 reasons for the subjects' food choices.

### 159 ***Subjective measurements***

160 Hunger and *liking* for each dish were evaluated as in EXP1. Questions asked at the end  
161 of the meal were as follows: 1) Did you find the presented foods pleasant? 2) Were the  
162 presented foods varied enough? 3) Did you have enough to eat? Participants were also asked  
163 if their food choices were made: 4) According to the pleasure expected? 5) According to the  
164 dietary recommendations associated with your illness? 6) According to the nutritional value  
165 that you think you needed? and 7) According to your state of hunger? Responses were  
166 evaluated using 10-cm VASs with the statement "very unpleasant/too little variety/not at all"  
167 and "very pleasant/very diversified/yes, absolutely".

168

### 169 ***Blood parameters***

170 All participants provided a blood sample (during the first session between 8:30 am and  
171 9:30 am) to measure plasma albumin, transthyretin, urea, creatinine and C-reactive protein.

172

### 173 ***STATISTICAL ANALYSES***

174 Values are expressed as the means  $\pm$  SDs. Delta values indicate the difference in a  
175 parameter between the early (7:30-8:00 am) and late morning (11:30 am-12:00 pm). Power  
176 sample calculation was determined, in EXP1 from the expected change in *wanting* according  
177 to our previous study (32) and in EXP2, from the mean change in *wanting* of protein-rich  
178 foods in EXP1. Differences between the two experimental sessions for the HD patients were  
179 analyzed with two-way repeated measure ANOVAs (factor A: days; factor B: times of  
180 measurement) and with one-way repeated measure ANOVAs for healthy subjects. Values for  
181 the HD patients (days with or without dialysis) and those for the healthy subjects at a given

182 time point were compared using one- or two-way ANOVAs (factor A: days; factor B: times  
183 of measurement). Whenever differences were significant, the Tukey *post hoc* test was applied.  
184 Anthropometric values, blood parameters and delta values were compared with Student's t-  
185 tests or the Mann-Whitney U-test. Spearman's correlation tests were used to screen for links  
186 between data. SigmaStat software (version 3.1, Systat Software Inc., Richmond, CA, USA)  
187 was used for analyses. Pearson's principal component analysis (PCA), with a correlation  
188 threshold at  $P < 0.02$ , was done using XLSTAT software (version 2015, Addinsoft Inc., New  
189 York, USA). Statistical significance was set at  $P < 0.05$ .

190

## 191 **RESULTS**

### 192 ***EXPI***

#### 193 ***Participants' characteristics (Table 1)***

194 There were no significant differences between HD patients and healthy subjects for  
195 sex, age and BMI. Participants' mean body weight was stable during the six months preceding  
196 the study.

197 In HD patients, compared to healthy subjects: hemoglobin levels were lower; albumin,  
198 protein, calcium and potassium concentrations in plasma were similar and; transthyretin, C  
199 reactive protein and serum phosphorus were higher.

200 Additional individual characteristics of HD patients are provided in Supplemental  
201 Material 2.

#### 202 ***Attitude towards food and usual food intake (Table 2)***

203 HD patients were more restricted and less disinhibited than healthy subjects. They  
204 were also less hungry overall.

205 Usual daily energy intake and fat intake did not differ between groups, whereas  
206 protein and carbohydrate intakes were lower in HD patients than in healthy subjects.

207 ***Hunger, liking and wanting***

208           Hunger was more intense at 11:30 am than at 7:30 am in all participants (**Figure 1**). At  
209 7:30 am, HD patients had similar levels of hunger on days with and without dialysis, but  
210 hunger was greater in HD patients than in healthy subjects on the dialysis day. At 11:30 am,  
211 hunger was similar in all participants.

212           *Liking* for protein-rich foods increased from 7:30 am to 11:30 am in HD patients and  
213 in healthy subjects (**Figure 2A**), whereas *liking* for fat-rich foods increased only in healthy  
214 subjects (**Figure 2B**) and *liking* for carbohydrate-rich foods did not change (**Figure 2C**).  
215 *Liking* for the three types of nutrients did not differ significantly between the participants at  
216 7:30 am and at 11:30 am.

217           *Wanting* increased from 7:30 am to 11:30 whatever the participants' condition and the  
218 type of macronutrient (**Figure 3ABC**). At 7:30 am, there were no significant differences  
219 between HD patients and healthy subjects whatever the macronutrient. By contrast, at 11:30  
220 am, *wanting* for protein-rich foods was lower on the day without than on the day with  
221 dialysis, and was lower than *wanting* reported by hemodialysis (**Figure 3A**). Consequently,  
222 *wanting* for protein at 11:30 am was similar in HD patients after dialysis and in healthy  
223 subjects. HD patients exhibited similar levels of *wanting* for fat and carbohydrate at 11:30 am  
224 whether they underwent dialysis or not (**Figure 3BC**). Finally, at 11:30 am, healthy subjects  
225 showed higher *wanting* for fat-rich foods than did HD patients on days with and without  
226 dialysis (**Figure 3B**).

227

228 ***Blood parameters (Table 3)***

229           The mean plasma concentration of ghrelin was higher in HD patients at 8:00 am than  
230 at 11:00 am, and also higher than the concentration measured at 8:00 am in healthy subjects.  
231 The mean plasma leptin concentration decreased from 8:00 am to 11:00 am for all  
232 participants, particularly for HD patients. The mean plasma insulin concentration decreased  
233 from 8:00 am to 11:00 am for all participants.

234           From 8:00 am to 11:00 am, plasma AA concentrations decreased in HD patients and  
235 healthy subjects. Delta values indicated greater decreases in HD patients than in healthy  
236 subjects for glutamine, citrulline, cysteine, histidine, 1-3 methyl-histidine, lysine, arginine and  
237 proline. In contrast, smaller decreases were found in HD patients than in healthy subjects for  
238 plasma aspartic acid, serine and glutamine. Only tryptophan was lower in HD patients than in  
239 healthy subjects for both time points. Finally, at 8:00 am, mean citrulline, 1-3 methyl-  
240 histidine concentrations were higher in HD patients than in healthy subjects, while at 11:00  
241 am, mean lysine and arginine concentrations were lower in HD patients.

242 ***Correlations between wanting for protein-rich foods and other parameters***

243           In HD patients, the increase in *wanting* for protein-rich foods from 7:30 am to 11:30  
244 am correlated with the decrease in plasma concentrations of glutamine ( $r=0.457$ ,  $P< 0.05$ ),  
245 alanine ( $r=0.559$ ,  $P< 0.01$ ), citrulline ( $r=0.422$ ,  $P< 0.05$ ), ornithine ( $r=0.591$ ,  $P< 0.01$ ) and  
246 proline ( $r=0.675$ ,  $P< 0.001$ ) and with the global decrease in plasma AAs (sum of all AAs)  
247 ( $r=0.574$ ,  $P< 0.01$ ). Conversely, the increase in *wanting* for protein-rich foods did not  
248 correlate with changes in plasma concentrations of ghrelin, leptin and insulin, hunger, overall  
249 *liking* and *wanting* for fat- and carbohydrate-rich foods.

250           In contrast, the increase in *wanting* for protein-rich foods in healthy subjects from 7:30  
251 am to 11:30 am did not correlate with changes in plasma concentrations of AAs (taken  
252 individually or together) or plasma hormones, but it did correlate with an increase in hunger

253 ( $r=0.757$ ,  $P<0.001$ ), *liking* for protein-rich foods ( $r=0.695$ ,  $P<0.01$ ) and *wanting* for fat-  
254 ( $r=0.553$ ,  $P<0.05$ ) and carbohydrate-rich foods ( $r=0.813$ ,  $P<0.001$ ).

255 When all variables, including hunger, *liking*, *wanting*, plasma ghrelin, leptin, insulin  
256 and AAs, were put into a principal component analysis there was a clear difference between  
257 HD patients and healthy subjects in *wanting* for protein-rich foods. In HD patients, *wanting*  
258 for protein-rich foods was mainly associated with the concentration of plasma AAs and not  
259 with hunger or *liking* or *wanting* for other types of foods (**Figure 4A**). The contrary was  
260 observed in healthy subjects (**Figure 4B**).

## 261 ***EXP2***

### 262 ***Participants' characteristics (Table 4)***

263 HD patients and healthy subjects were similar in terms of sex, age and BMI.  
264 Participants' mean body weight was stable during the six months preceding the study.

265 Plasma albumin was lower in HD patients than in healthy subjects, whereas  
266 transthyretin was similar in both groups. C-reactive protein was higher in HD patients than in  
267 healthy subjects (Table 4).

268 The mean normalized protein catabolic rate (nPCR) was  $1.03\pm 0.4$  g/kg/day, and mean  
269 KT/V was  $1.38\pm 0.27$  g/kg/day.

### 270 ***Hunger and liking before the meal***

271 Hunger at about 12:30 pm was similar in all participants (**Figure 5**).

272 HD patients (days with and without dialysis) and healthy subjects showed similar  
273 *liking* for protein-, carbohydrate- and fat-rich dishes, but the low-energy dish (ratatouille) was  
274 preferred by healthy subjects (Table 5).

### 275 ***Food intake from the buffet (Table 6 and Figure 6)***

276 HD patients ate more protein on the day with than on the day without dialysis, but  
277 there was no significant difference in energy, fat or carbohydrate intake between the two days.



278 The ratio of energy intake from protein was therefore higher just after dialysis than on the day  
279 without dialysis, while it was slightly lower for carbohydrates.

280 In healthy subjects, energy intake was lower than in HD patients. Healthy subjects  
281 consumed less protein than HD patients after dialysis and less fat than HD patients on both  
282 days. Carbohydrate intake was similar in all participants (healthy subjects and HD patients).

### 283 *Postprandial hunger and liking for the eight dishes*

284 After lunch, hunger was similar in all participants (**Figure 5**).

285 Compared with healthy subjects, HD patients reported a persistent higher *liking* for  
286 roast chicken after the meal on the dialysis day and, a lower *liking* for ratatouille on the day  
287 without dialysis (Table 5).

288 According to the questionnaires, the pleasantness procured by the foods, the variety of  
289 the dishes, the quantity proposed and the reasons for the subjects' choices were rated equally  
290 by all participants. The only difference was that healthy subjects were more likely to make  
291 food choices for hedonic reasons.

292

## 293 **GENERAL DISCUSSION**

294 This study showed that dialysis induced a significant increase in *wanting* for protein,  
295 which was higher on days with than on days without dialysis, bringing it up to levels seen in  
296 healthy subjects. This increase in the desire to eat protein-rich foods was confirmed by a  
297 significant increase in spontaneous protein intake just after dialysis.

298 In EXP1, according to the TFEQ, HD patients had a significantly more restrictive, less  
299 disinhibited and less hungry psychological profile than the healthy subjects, probably due to  
300 the dietary constraints usually required (33, 34). However, energy intake did not differ  
301 significantly between HD patients and healthy subjects. Furthermore, neither group showed  
302 significant PEW (similar BMI, weight and plasma albumin), although protein intake was

303 slightly lower in HD patients and even though previous studies have shown that PEW is  
304 common in CKD patients (2, 3). As hunger at 11:30 am was similar in all participants, the  
305 observed changes in eating approaches, particularly in *wanting* for protein, cannot be related  
306 to differences in this parameter.

307 Before lunch, *wanting* for protein-rich foods in HD patients differed from that in  
308 healthy subjects. To our knowledge, decreased *wanting* for protein on days without dialysis  
309 (*i.e.*, at midday on the day between usual dialysis sessions) and the return to a normal level  
310 immediately after dialysis have never been reported. This lower *wanting* for protein 24 h  
311 before and increased *wanting* after dialysis indicates a change in the food reward system and  
312 reinforces data on changes in food preferences observed in HD patients: reduced preference  
313 for sweet food and refusal of red meat (28-31).

314 The increase in the desire to eat protein after dialysis (*i.e.* the increase in protein  
315 *wanting*) was confirmed by the results of EXP2. At lunch immediately after dialysis, the  
316 spontaneous *ad libitum* intake of protein in HD patients was higher than that in healthy  
317 subjects and higher than their own intake on the day without dialysis. It should be highlighted  
318 that differences in hunger cannot explain the increased protein intake after dialysis, as levels  
319 were similar before lunch for all participants.

320 There is an established link between impaired renal function and a gradual reduction  
321 in food consumption (27, 35). Decreased energy intake and protein-energy metabolic  
322 abnormalities appear to be the two main factors contributing to PEW in CKD patients (8).  
323 Though there are some benefits to increasing protein intake on days with dialysis (33-41), the  
324 present study supports the idea that protein-rich foods should be provided after dialysis since  
325 they are more appealing at that time (36-39). To our knowledge, no studies have observed an  
326 increase in the *wanting* and spontaneous intake of protein-rich foods after dialysis, but it  
327 should be noted that the use of protein-enriched meals during dialysis has been reported with

328 beneficial effects. Indeed, in hypoalbuminemic hemodialysis patients, high-protein meals  
329 during dialysis combined with a potent phosphorus binder increases serum albumin while  
330 controlling phosphorus (40) and, patients report positive attitudes toward receiving high-  
331 protein-meals during dialysis without increasing symptomatic hypotension events (41).  
332 Further studies could compare the effect of protein-rich foods during and after dialysis on the  
333 food reward system and the nutritional status of HD patients.

334         The post-dialysis increases in *wanting* for protein does not seem to be a consequence  
335 of variations in plasma ghrelin, leptin and insulin concentrations since: 1) there was no  
336 correlation between increases in *wanting* for protein from 8:00 am to 11:00 am and changes in  
337 plasma hormone concentrations were observed; 2) principal component analyses showed very  
338 different statistical relationships between study outcomes for HD patients and healthy subjects  
339 for plasma ghrelin, leptin and insulin.

340         The post-dialysis increases in *wanting* for protein and protein consumption could be  
341 related to the change in plasma AAs. Fluctuations in plasma AAs may simultaneously affect  
342 the reward system, food motivation and food choices with an appetite for or a rejection of  
343 proteins (27, 42). These fluctuations can also influence the intake of protein-rich foods to  
344 restore or maintain an adequate protein status (43). In the present study, there was a  
345 significant decrease in almost all AAs during dialysis. As already shown by Boirie et al., loss  
346 of kidney function may also impair the conversion of some AAs, such as the conversion of  
347 phenylalanine to tyrosine (44). Therefore, the hemodialysis-mediated decrease in some AAs  
348 may remove the physiological “brake” they exert on *wanting* for protein when their  
349 concentrations are high. Principal component analyses support this interpretation (the increase  
350 in *wanting* for protein at lunch just after dialysis correlated only with decreases in plasma AA  
351 concentrations).

352           It is difficult to clarify the influence of each AA on the increase in *wanting* for protein  
353 after dialysis. Plasma tryptophan (Trp) could play a role. It was the only plasma AA whose  
354 concentrations were lower in HD patients than in healthy subjects at both 8:00 am and 11:00  
355 am, as already reported (27, 45). Animal and human studies have shown that increases in  
356 plasma tryptophan concentrations or in the plasma tryptophan/large neutral AAs (*i.e.*, valine,  
357 isoleucine, leucine, phenylalanine, and tyrosine) ratios are related to increases in tryptophan  
358 concentrations in the central nervous system (42, 46, 47). This imbalance could interfere with  
359 the passage of hemato-meningeal branched-chain amino acids and Trp, with a subsequent  
360 increase in serotonin synthesis leading to anorexia (45). Further analysis of aminograms from  
361 dialysis liquids should help to determine the influence of each AA in the post-dialysis  
362 increase in *wanting* for protein.

363           For the purpose of this proof-of concept study, we deliberately selected a small  
364 number of homogenous patients without diabetes (diabetic patients often follow a restrictive  
365 diet that can modify their spontaneous feeding behavior, their taste perception and their food  
366 preferences). Consequently, these results cannot be generalized to all hemodialysis patients in  
367 particular to older and diabetic subjects, before supplemental experimental observations.  
368 Furthermore, as the present study was conducted over a short period it would be relevant to  
369 evaluate the long-term effect of protein supplementation just after dialysis to evaluate the  
370 acceptance of such diet and its effect on nutritional status in particular in HD patients with  
371 PEW assessed by the standard methods of SGA or Malnutrition Inflammation Score. Strength  
372 of the present study is the confirmation of the desire to eat protein-rich foods after dialysis as  
373 noted in EXP.1, under real-life conditions during a lunch buffet in uninformed subjects as  
374 observed in EXP. 2. In contrast, a limitation of the study consists in the absence of  
375 measurement of plasma AAs on the interdialytic interval day in Exp. 1 (initially, authors

376 estimated that it was neither desirable nor ethical to take two blood samples on these days to  
377 avoid blood vessel break-ins).

378

379 In conclusion, the feeding behavior of HD patients changed immediately after  
380 hemodialysis, and probably during the dialysis given the anticipation of the amino acid  
381 depletion that happened with hemodialysis treatment, with significant increases in both  
382 *wanting* for and spontaneous *ad libitum* consumption of protein. These changes appear to be  
383 related to per-dialysis changes in plasma AA concentrations and not to variations in plasma  
384 ghrelin, leptin or insulin concentrations. This observation suggests that a post-dialysis meal of  
385 protein-rich food might be a key opportunity for HD patients to increase protein intake,  
386 nutritional status, quality of life and survival.

387

### 388 **Practical Application:**

- 389 • Protein-energy wasting is a risk factor for mortality and complications in hemodialysis  
390 patients
- 391 • The appetite/incentive motivation (*i.e.* the *wanting* component of the reward system)  
392 to eat protein-rich foods and the spontaneous *ad libitum* intake of protein-rich foods in  
393 real condition are high immediately after dialysis
- 394 • Increases in *wanting* and spontaneous intake of protein-rich foods correlated with the  
395 decrease in plasmatic amino acids concentrations by dialysis
- 396 • PEW could be prevented in HD patients by protein intake during and immediately  
397 after haemodialysis

398

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531

## 532 LEGENDS FOR FIGURES

533 **Figure 1.** Hunger sensation in 24 healthy subjects and in 24 hemodialysis patients on a dialysis  
534 day or an interdialytic interval day in Experiment 1.

535 Hunger was evaluated at 7:30 am and at 11:30 am, before and after the dialysis (50% of the  
536 patients were evaluated the day before and 50% the day after dialysis) or at an identical time  
537 when no dialysis was performed. Participants indicated their hunger sensation using a 10-cm  
538 visual analog scale. Values are means  $\pm$  SDs. Hunger was higher at 11:30 am than at 7:30 am  
539 in healthy subjects ( $P < 0.001$ ) and in hemodialysis patients ( $P < 0.001$ ). At 7:30 am, hunger  
540 was similar in hemodialysis patients on both days but was higher in hemodialysis patients on  
541 the dialysis day than it was in healthy subjects ( $P < 0.05$ ). At 11:30 am, hunger was similar in  
542 all subjects. \* and \*\*\* indicate significant differences ( $P < 0.05$  and  $P < 0.001$ , respectively).

543

544 **Figure 2.** The degree of *liking* of protein-, fat- and carbohydrate-rich foods in 24 healthy  
545 subjects and in 24 hemodialysis patients on a dialysis day or an interdialytic interval day in  
546 Experiment 1.

547 *Liking* (*i.e.*, the pleasantness induced by foods) was evaluated at 7:30 am and at 11:30 am for  
548 each food after smelling 2 protein-rich foods [Bündnerfleisch (dried beef) and imitation crab  
549 meat – Figure 2A], 2 fat-rich foods (melted butter and mayonnaise – Figure 2B) and 2  
550 carbohydrate-rich foods (honey and strawberry jam – Figure 2C). *Liking* was evaluated using  
551 10-cm VAS. Values are means  $\pm$  SDs. The degree of *liking* of protein-rich foods increased  
552 from 7:30 am to 11:30 am in healthy subjects ( $P < 0.001$ ) and in hemodialysis patients  
553 ( $P < 0.05$ ). The degree of *liking* of fat-rich foods increased from 7:30 am to 11:30 am only in  
554 healthy subjects ( $P < 0.05$ ). The degree of *liking* for carbohydrate-rich foods did not change  
555 from 7:30 am to 11:30 am in healthy subjects and in hemodialysis patients. No significant

556 difference in *liking* for each macronutrient was noted at 7:30 am and at 11:30 am in healthy  
557 subjects and hemodialysis patients.

558

559 **Figure 3.** The degree of *wanting* of protein, fat- and carbohydrate-rich foods in 24 healthy  
560 subjects and in 24 hemodialysis patients on a dialysis day or an interdialytic interval day in  
561 Experiment 1.

562 *Wanting* was evaluated at 7:30 am and at 11:30 am according to the desire to eat 6 protein-  
563 rich foods presented on separate pictures (fried eggs, grilled salmon, baked chicken, veal  
564 steak, rib steak and turkey breast – Figure 3A), 6 fat-rich foods presented on separate pictures  
565 (avocados, olives, peanuts, chocolate, fried fritters and whipped cream – Figure 3B) and 6  
566 carbohydrate-rich foods presented on separated pictures (potato puree, rice, lentils, apples,  
567 pasta, and fruit cake – Figure 3C). *Wanting* was evaluated using 10-cm VAS. Values are  
568 means  $\pm$  SDs. The degree of *wanting* of protein-, fat- and carbohydrate-rich foods increased  
569 from 7:30 am to 11:30 am in healthy subjects and in hemodialysis patients ( $P < 0.001$  for all).  
570 A significant interaction and Tukey's *post hoc* tests indicated that the hemodialysis patients'  
571 *wanting* of protein-rich foods at 11:30 am was lower on the interdialytic day ( $P < 0.01$ ) than it  
572 was on the dialysis day, and it was also lower ( $P < 0.001$ ) than that of healthy subjects. No  
573 difference was observed in the degree of fat and carbohydrate *wanting* at 11:30 am on days  
574 with or without dialysis. Higher *wanting* of fat-rich foods was also noted in healthy subjects  
575 compared with that of hemodialysis patients both on the dialysis day and on the interdialytic  
576 interval day ( $P < 0.05$ , for both). \*, \*\* and \*\*\* indicate  $P < 0.05$ ,  $P < 0.01$  and  $P < 0.001$ ,  
577 respectively.

578

579 **Figure 4.** Principal component analysis with the variations of the measured parameters from the  
580 early to late morning (delta values) in 24 healthy subjects and 24 hemodialysis patients on a  
581 dialysis day in Experiment 1.

582 The principal component discriminates between the influences of the different parameters  
583 measured by the *wanting* of protein-rich foods (the desire to eat protein-rich foods after  
584 presentation of 8 pictures) in hemodialysis patients on the day of dialysis (Figure 4A) and in  
585 healthy subjects (Figure 4B). In hemodialysis patients, *wanting* (*W*) of protein-rich foods  
586 mainly correlated with a decrease in plasma amino acid concentrations but not with hunger  
587 sensation, *liking* (*L*) of protein, fat or carbohydrates, *wanting* of fat- and carbohydrate-rich  
588 foods or plasma leptin or insulin concentrations. In healthy subjects, *wanting* of protein-rich  
589 foods was positively related to hunger sensation, *liking* of all foods (proteins, fat and  
590 carbohydrates), and *wanting* of fat- and carbohydrate-rich foods; it was negatively correlated  
591 with plasma leptin and insulin concentrations but not with plasma amino acid concentrations.  
592

593 **Figure 5.** Hunger sensation in 18 healthy subjects and in 18 hemodialysis patients on a  
594 dialysis day and on an interdialytic interval day before and after meal ingestion from a lunch  
595 buffet in Experiment 2.

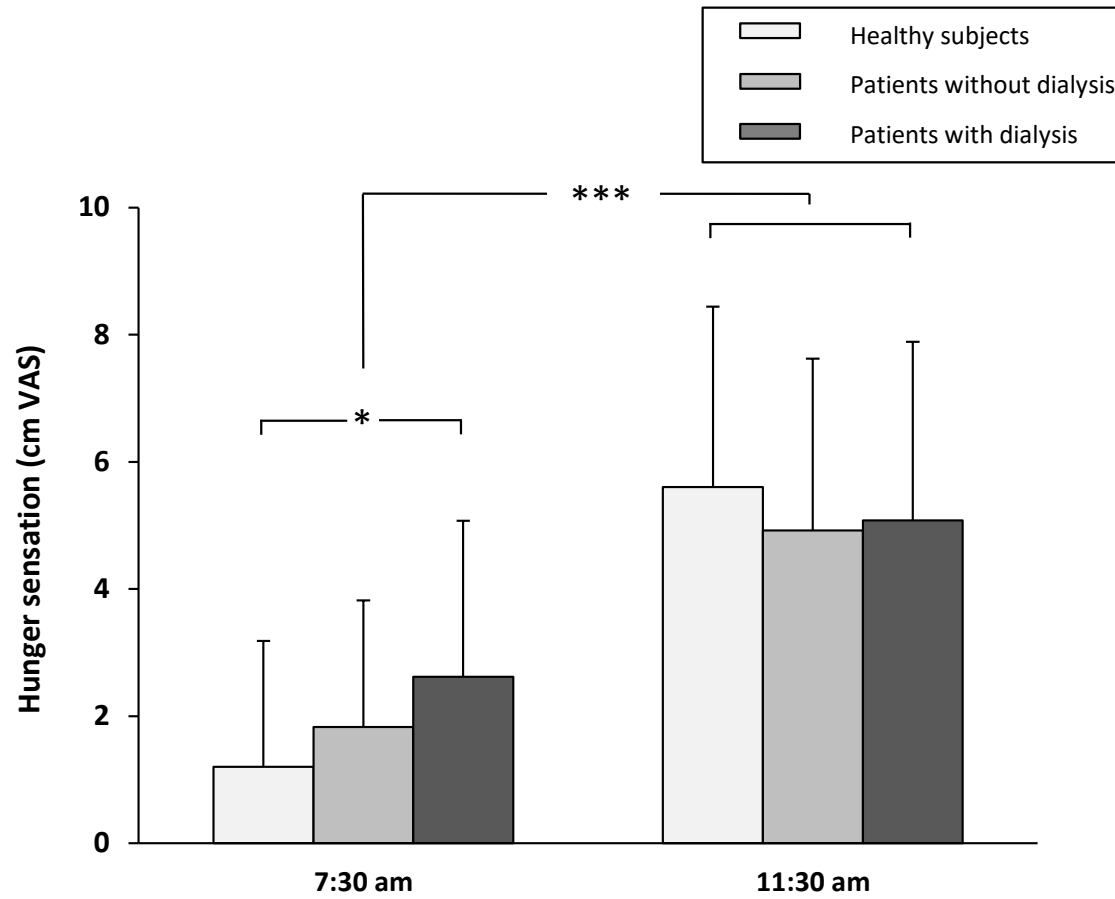
596 Hunger was evaluated before and after a buffet composed of 8 courses (roast chicken, roast beef,  
597 smoked salmon rolled in St-Môret cheese, tuna and tomato salad, mayonnaise, cream of lentil  
598 soup, ratatouille and black cherries baked in a batter), using a 10-cm visual analog scale.

599 Participants were able to eat each of the foods of their choice in the quantities they desired, and  
600 they were unaware of the objectives of the study. Values are means  $\pm$  SD. Hunger decreased  
601 after ingestion of the meal in healthy subjects ( $P < 0.001$ ) and in hemodialysis patients ( $P <$   
602  $0.001$ ).

603

604 **Figure 6.** Protein, fat and carbohydrate intake (g) from an 8-course lunch buffet served to 18  
605 healthy subjects and 18 hemodialysis patients on a dialysis day and on an interdialytic interval  
606 day in Experiment 2.  
607 Values are means  $\pm$  SD. Protein intake was higher just after dialysis than it was on an  
608 interdialytic interval day ( $P < 0.01$ ) but intakes of fat and carbohydrates were similar. Healthy  
609 subjects ate less protein than the hemodialysis patients did just after dialysis ( $P < 0.05$ ), and they  
610 ate less fat ( $P < 0.01$ ) but similar amounts of carbohydrates as hemodialysis patients in general.

Figure 1:





**Figure 2:**

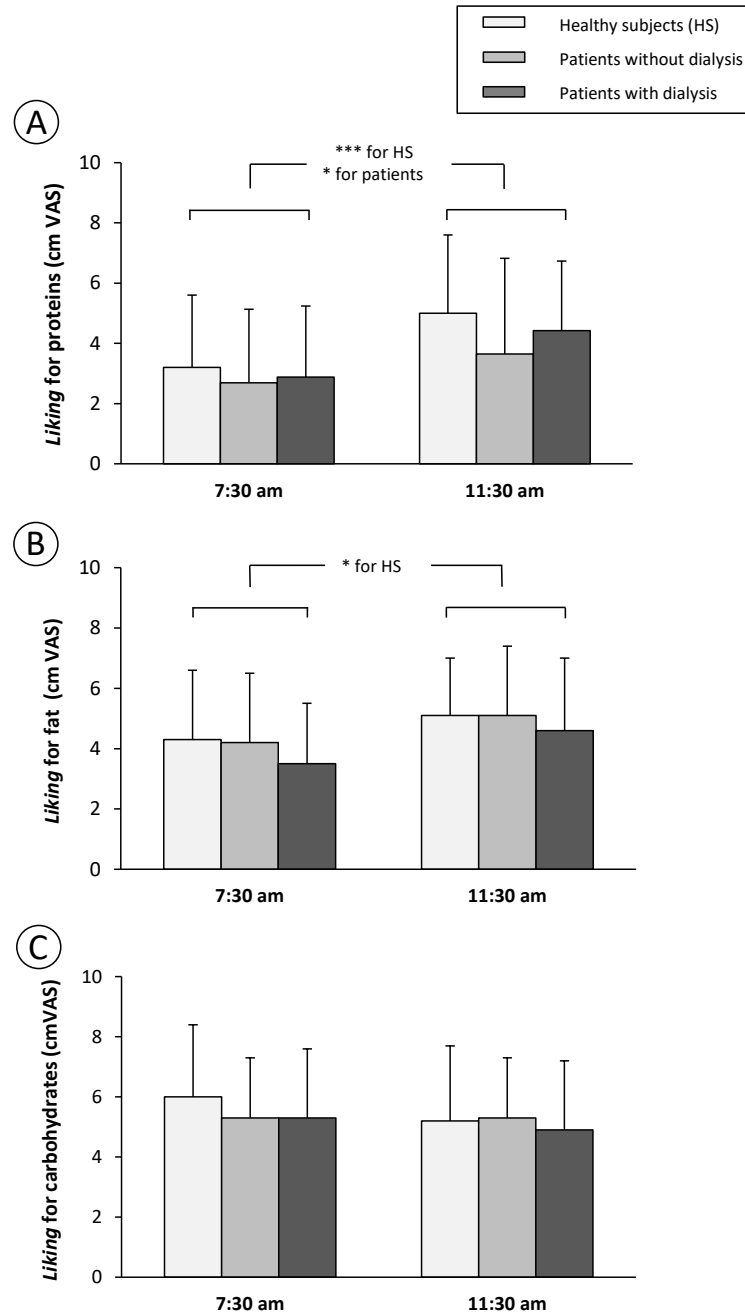


Figure 3:

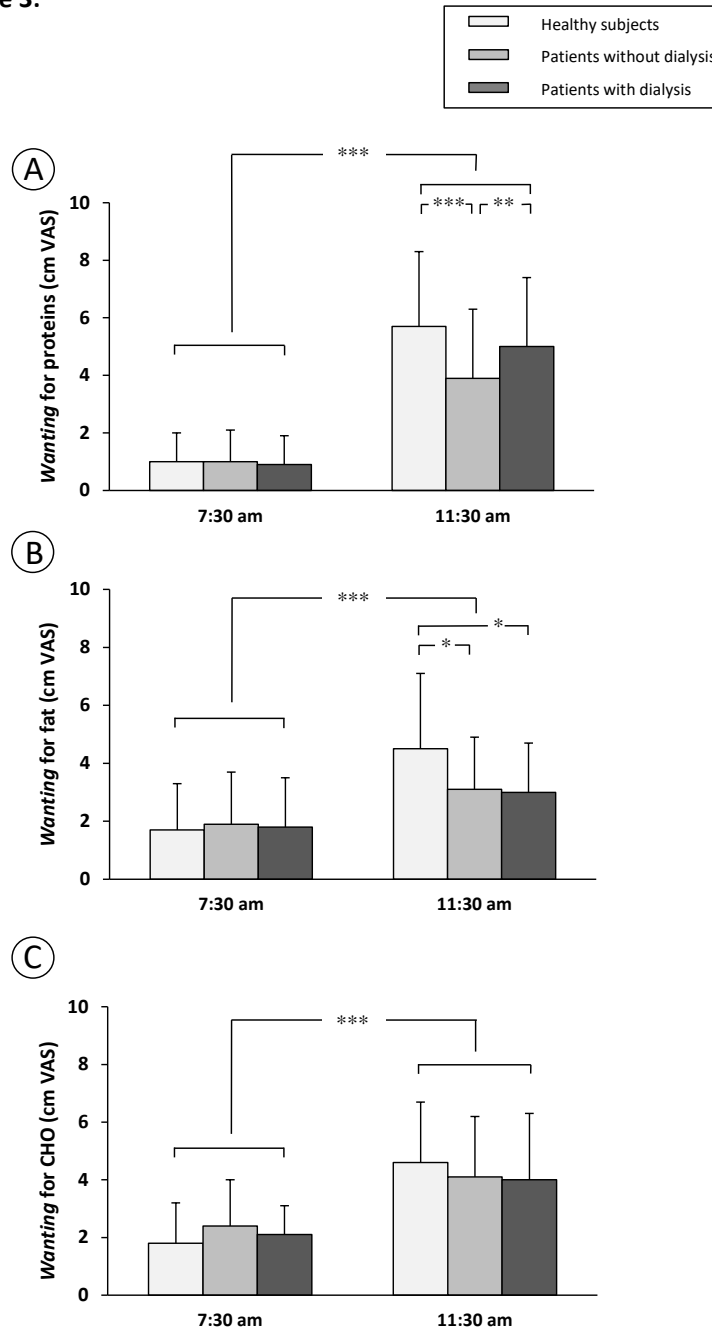


Figure 4:

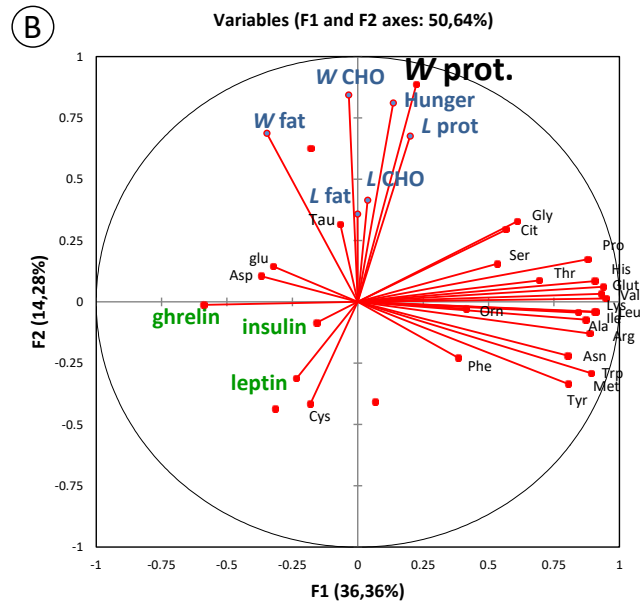
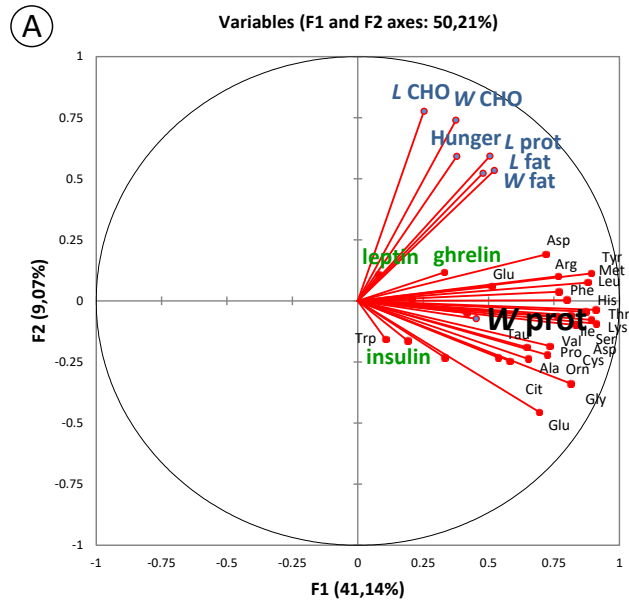


Figure 5:

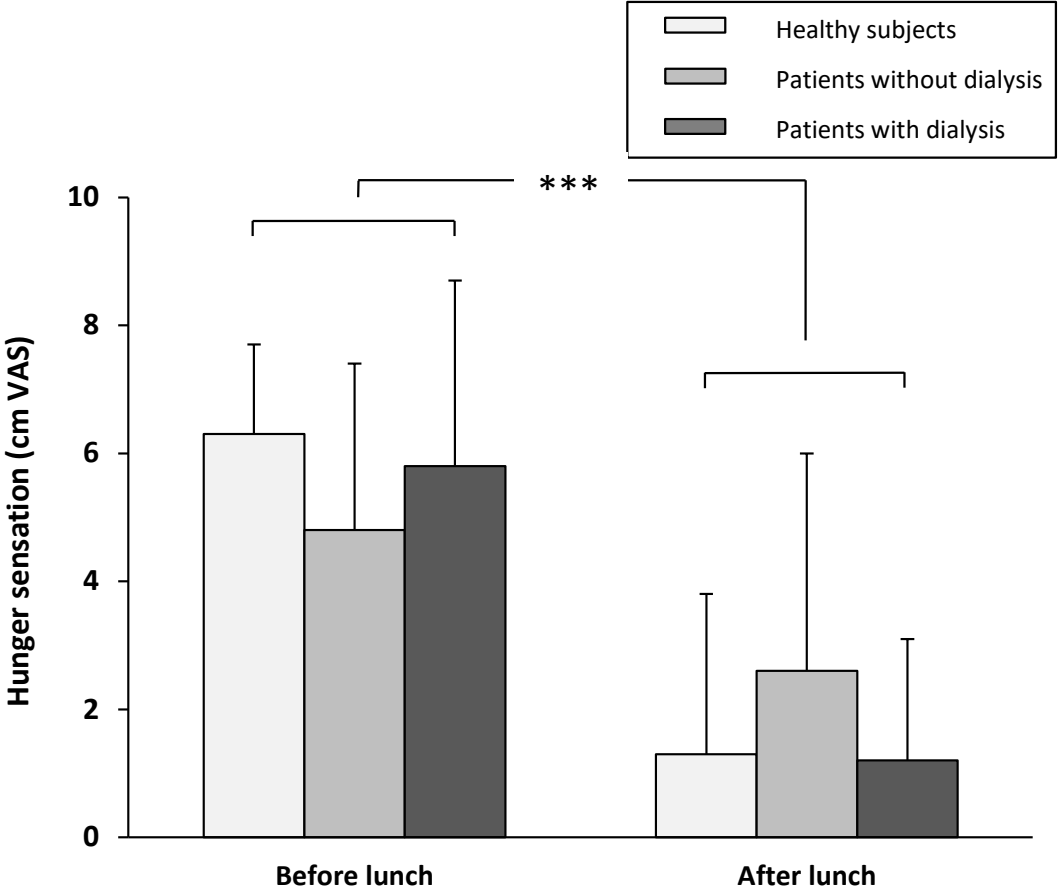
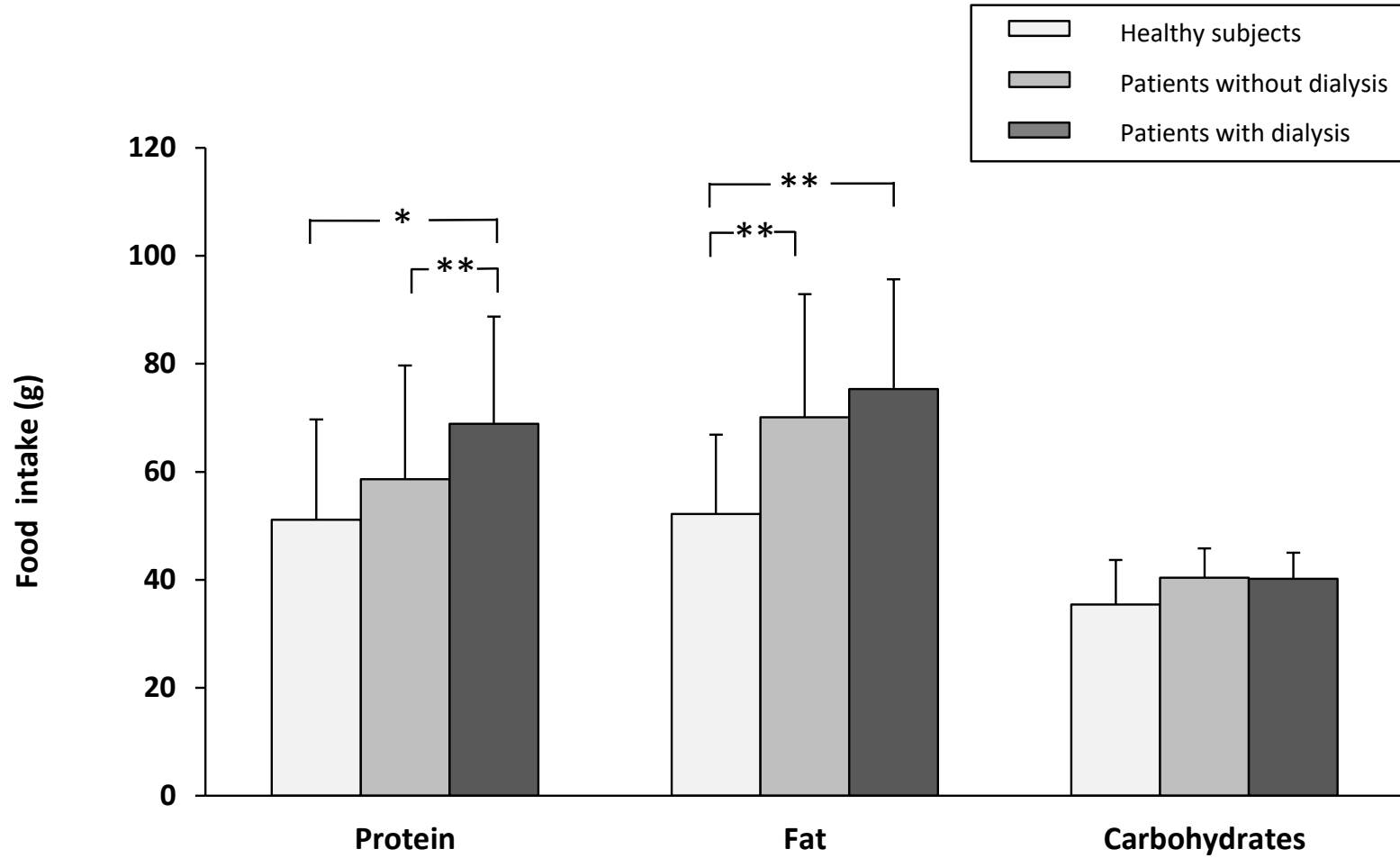


Figure 6:



1 **Table 1:** Anthropometric characteristics and blood parameters in 24 healthy subjects and 24  
 2 hemodialysis patients before dialysis in Experiment 1.

3

	Healthy subjects	Hemodialysis patients
Sex (male/female)	7/17	7/17
Age (years)	59 ± 14	61 ± 13
Weight (kg)	76.2 ± 14.3	74.0 ± 16.5
Body mass index (kg.m <sup>-2</sup> )	25.11 ± 3.42	25.85 ± 5.35
Hemoglobin (g/100 mL)	13.9 ± 1.3	11.7 ± 1.3***
Albumin (g/L)	38.6 ± 5.3	36.5 ± 7.0
Transthyretin (g/L)	0.270 ± 0.063	0.334 ± 0.097**
Protein (g/L)	72 ± 6	71 ± 8
Urea (mmol/L)	6.4 ± 1.9	24.4 ± 8.6***
Creatinine (µmol/L)	78 ± 15	847 ± 184***
Creatinine clearance (mL/min)	90.2 ± 15.7	5.2 ± 1.4***
Potassium (mmol/L)	4.1 ± 0.4	4.4 ± 0.6
Calcium (mmol/L)	2.21 ± 0.12	2.22 ± 0.18
Phosphorus (mmol/L)	1.02 ± 0.18	1.60 ± 0.50***
C-reactive protein (mg/L)	2.6 ± 5.6	16.0 ± 20.2***

4

5 Blood samples were taken at approximately 8:00 am. All values are means ± SDs. The Mann-  
 6 Whitney U-test indicates significant differences between hemodialysis patients and healthy  
 7 subjects (\*\* and \*\*\* symbolize P < 0.01 and P < 0.001, respectively).

1 **Table 2:** Attitude towards food according to the Three-Factor Eating Questionnaire (TFEQ)  
 2 and mean daily food intake from a 3-day dietary survey of 24 healthy subjects and 24  
 3 hemodialysis patients in Experiment 1.

	Healthy subjects	Hemodialysis patients
TFEQ – restriction	6.8 ± 3.7	9.1 ± 3.8*
TFEQ – disinhibition	6.0 ± 3.5	3.7 ± 1.7**
TFEQ – hunger	3.8 ± 3.0	1.8 ± 1.9*
Total energy intake (kJ/d)	7163 ± 427	6937 ± 2280
(kcal/d)	1712 ± 102	1658 ± 545
(kcal/kg)	23.2 ± 4.5	22.8 ± 7.2
Protein intake (kcal/d)	302 ± 25	277 ± 76*
(g/d)	76 ± 6	69 ± 19*
(% of energy intake)	17.7 ± 0.7	17.1 ± 2.5
(g/kg bodyweight)	1.03 ± 0.20	0.96 ± 0.25
Carbohydrate intake (kcal/d)	829 ± 49	757 ± 304*
(g/d)	207 ± 12	189 ± 76*
(% of energy intake)	48.5 ± 1.8	44.9 ± 4.8**
Fat intake (kcal/d)	578 ± 45	626 ± 202
(g/d)	64 ± 5	70 ± 22
(% of energy intake)	33.8 ± 1.7	38.1 ± 4.2***

4 Before the experimental sessions, participants completed the TFEQ to evaluate their attitude  
 5 toward food according to three dimensions (dietary restriction, disinhibition and hunger).  
 6 After the experimental sessions, a dietary survey was conducted by a dietitian to assess  
 7 participants' usual 24 h dietary intake. All values are means ± SDs. The Mann-Whitney U-test  
 8 indicates significant differences between hemodialysis patients and healthy subjects (\* and \*\*  
 9 symbolize P < 0.05 and P < 0.01, respectively).

1 **Table 3:** Hormones and plasma amino acid profiles in 24 healthy subjects and 24 in  
 2 hemodialysis patients in Experiment 1.

	Healthy subjects		Hemodialysis patients		Statistics
	8:00 am (A)	11:00 am (B)	8:00 am (C)	11:00 am (D)	
Ghrelin (pg/mL)	626 ± 361	890 ± 426	1659 ± 1191	974 ± 710	A-C* & C-D**
Leptin (ng/mL)	12.3 ± 12.9	11.8 ± 13.6	40.0 ± 45.4	25.6 ± 29.8	(1) and C-D***
Insulin (mUI/L)	28.7 ± 47.2	3.8 ± 5.5	30.1 ± 25.3	7.4 ± 7.5	(1)
Amino acids (nmol/ml)					(1)
Glycine	324.3 ± 91.8	256.8 ± 78.6	304.6 ± 147.2	217.4 ± 85.0	
Alanine	596.7 ± 205.5	418.1 ± 144.4	450.5 ± 260.8	235.8 ± 131.2	
Serine	166.4 ± 44.1	121.2 ± 31.4	105.0 ± 31.7	80.0 ± 19.4	A-B* & C-D***
Threonine	164.6 ± 63.8	131.6 ± 41.1	121.7 ± 50.6	75.0 ± 28.8	
Valine	356.8 ± 104.8	292.1 ± 78.0	235.5 ± 49.4	153.7 ± 26.6	
Isoleucine	96.4 ± 40.6	69.5 ± 20.4	73.5 ± 26.4	52.3 ± 19.5	
Leucine	194.1 ± 74.5	145.5 ± 37.1	123.6 ± 33.8	96.4 ± 25.6	
Lysine	247.4 ± 79.5	215.1 ± 71.4	183.5 ± 58.3	110.2 ± 39.8	B-D* & C-D***
Arginine	114.1 ± 32.2	119.7 ± 22.9	109.8 ± 31.3	76.1 ± 26.2	B-D* & C-D***
Histidine	107.8 ± 29.0	90.4 ± 22.5	81.3 ± 25.3	49.1 ± 12.6	C-D***
Tyrosine	97.7 ± 33.2	76.4 ± 27.7	55.8 ± 17.3	35.0 ± 11.6	
Phenylalanine	90.7 ± 27.9	71.1 ± 16.1	79.0 ± 21.6	58.1 ± 15.5	
Tryptophan	78.0 ± 23.5	50.3 ± 14.7	34.7 ± 13.2	16.2 ± 6.8	(2)
Methionine	40.3 ± 12.5	27.7 ± 8.0	27.8 ± 8.0	19.3 ± 6.3	
Cysteine	43.2 ± 22.6	22.8 ± 6.8	78.0 ± 29.1	17.8 ± 6.7	C-D***
Proline	331.6 ± 102.0	247.2 ± 60.3	431.5 ± 174.7	231.4 ± 83.8	C-D***
Glutamine	669.7 ± 184.4	609.8 ± 172.4	622.5 ± 267.5	404.6 ± 141.6	C-D***
Glutamic acid	92.2 ± 46.5	48.4 ± 28.1	118.8 ± 75.3	105.0 ± 39.9	
Asparagine	92.0 ± 27.4	72.9 ± 20.1	74.0 ± 22.0	48.2 ± 16.2	
Aspartic acid	26.4 ± 11.7	16.2 ± 9.9	24.0 ± 9.8	21.9 ± 8.0	
Citrulline	42.2 ± 17.0	40.1 ± 9.9	99.8 ± 38.3	41.7 ± 12.7	A-C*** & C-D***
Ornithine	113.5 ± 29.9	71.6 ± 27.6	109.9 ± 39.7	65.4 ± 31.2	
Taurine	192.2 ± 73.6	92.5 ± 29.1	169.2 ± 60.5	96.6 ± 58.3	

23

24 Blood samples were drawn at approximately 8:00 am in hemodialysis patients (when  
 25 connected to the hemodialysis apparatus) and were drawn again at approximately 11:00  
 26 (when disconnected from the hemodialysis apparatus). Blood was also collected at the same



27 time from healthy subjects. All values are means  $\pm$  SDs. Capital letters refer to the following:  
28 A, healthy subjects - 8:00 am; B, healthy subjects - 11:00 am; C, hemodialysis patients - 8:00  
29 am; and D, hemodialysis patients - 11:00 am. Two-way repeated measure ANOVAs indicate,  
30 1) significant decreases from 8:00 am to 11:00 for plasmatic concentrations of leptin  
31 ( $P < 0.01$ ), insulin ( $P < 0.001$ ) and all amino acid ( $P < 0.001$ , except  $P < 0.01$  for arginine), as  
32 showed by (1); 2) lower plasmatic concentration of tryptophan in hemodialysis patients  
33 compared with healthy subjects ( $P < 0.05$ ) as pointed by (2) and, 3) significant interactions  
34 highlighted with Tukeys' post hoc tests as represented by stars (\* and \*\*\* symbolize  $P < 0.05$   
35 and  $P < 0.001$ , respectively). For additional information on the statistical results, see  
36 supplemental material 3.

37

1 **Table 4:** Anthropometric characteristics and blood parameters in 18 healthy subjects and in  
 2 18 hemodialysis patients before dialysis in Experiment 2.

3

	<b>Healthy subjects</b>	<b>Hemodialysis patients</b>
Sex (male/female)	9/9	10/8
Age (years)	68 ± 12	69 ± 11
Weight (kg)	76.2 ± 14.3	74.0 ± 16.5
Body mass index (kg.m <sup>-2</sup> )	25.76 ± 4.35	26.04 ± 5.81
Albumin (g/L)	42.1 ± 2.4	37.7 ± 3.9**
Transthyretin (g/L)	0.286 ± 0.038	0.323 ± 0.083
Urea (mmol/L)	6.2 ± 0.9	A
Creatinine (µmol/L)	80 ± 13	A
Creatinine clearance (mL/min)	77.3 ± 11.3	A
C-reactive protein (mg/L)	1.9 ± 1.5	23.0 ± 52.4***

4

5 Healthy subjects were matched for sex, age and body mass index to hemodialysis patients.

6 Blood samples were drawn at approximately 9:00 am. All values are means ± SDs. The

7 Mann-Whitney U-test indicates significant differences between hemodialysis patients and

8 healthy subjects (\*\* and \*\*\* symbolize P < 0.01 and P < 0.001, respectively). “A” indicates

9 that these values were not pertinent in hemodialysis patients.

10

1 **Table 5:** *Liking* before and after intake of the 8 courses in 18 healthy subjects and in 18  
 2 hemodialysis patients just after dialysis and on an interdialytic day in Experiment 2.

3

	Healthy subjects	Hemodialysis patients without dialysis	hemodialysis patients after dialysis
<b>Before lunch</b>			
Roast chicken	6.1 ± 2.2	6.1 ± 2.4	7.0 ± 2.5
Roast beef	6.3 ± 1.4	6.0 ± 2.8	5.9 ± 3.0
Salmon rolled in cheese	5.6 ± 2.6	7.3 ± 2.6	6.7 ± 3.0
Tuna and tomato salad	5.2 ± 2.1	7.0 ± 2.3	6.5 ± 3.1
Mayonnaise	5.7 ± 1.8	5.9 ± 2.9	5.6 ± 3.1
Cream of lentil soup	7.2 ± 2.4	4.5 ± 3.3	5.4 ± 3.6
Black cherries baked in batter	6.8 ± 2.2	7.4 ± 2.5	7.3 ± 2.6
Ratatouille	6.4 ± 2.1 <sup>a</sup>	3.3 ± 3.0 <sup>a</sup>	4.6 ± 2.9
<b>After lunch</b>			
Roast chicken	3.9 ± 2.9 <sup>a</sup>	6.0 ± 2.5	6.6 ± 2.8 <sup>a</sup>
Roast beef	6.0 ± 3.6	4.9 ± 3.3	5.0 ± 3.2
Salmon rolled in cheese	5.1 ± 3.5	6.1 ± 2.1	5.8 ± 3.2
Tuna and tomato salad	6.6 ± 2.8	6.1 ± 2.9	6.6 ± 2.8
Mayonnaise	5.1 ± 3.7	4.9 ± 3.1	5.2 ± 3.4
Cream of lentil soup	5.5 ± 2.8	4.7 ± 3.2	4.6 ± 3.7
Black cherries baked in batter	7.6 ± 2.9	7.7 ± 2.3	7.5 ± 2.9
Ratatouille	5.8 ± 2.6 <sup>b</sup>	2.6 ± 2.6 <sup>b</sup>	3.9 ± 3.3

4

5 All values are means ± SDs. Results with the same letter next to them indicate that they are

6 significantly different. Then, before and after intake, ratatouille was less liked by

7 hemodialysis patients compared to healthy subjects on the interdialytic day ; after intake and

8 dialysis, a higher degree of *liking* for roast chicken persisted in hemodialysis patients

9 compared with healthy subjects (a and b indicates respectively,  $P < 0.05$  and  $P < 0.01$ ). For  
10 additional information on the statistical results, see supplemental material 3.  
11

**Table 6:** Food intake at an 8-course lunch buffet for 18 healthy subjects and 18 hemodialysis patients just after dialysis and on an interdialytic day in Experiment 2.

1

	Healthy subjects	Hemodialysis patients, interdialytic	hemodialysis patients, after dialysis
Energy intake (kJ)	3422 ± 900 <sup>a,f</sup>	4297 ± 1243 <sup>a</sup>	4661 ± 1063 <sup>f</sup>
(kcal)	816 ± 215 <sup>a,f</sup>	1027 ± 297 <sup>a</sup>	1114 ± 254 <sup>f</sup>
Protein intake (g)	51 ± 19 <sup>d</sup>	59 ± 21	69 ± 20 <sup>d,**</sup>
(% of energy intake)	24.6 ± 4.4	22.5 ± 3.5	24.6 ± 3.7 <sup>***</sup>
(g/kg bodyweight)	0.72 ± 0.32 <sup>d</sup>	0.84 ± 0.31	0.99 ± 0.29 <sup>d,**</sup>
Fat intake (g)	52 ± 15 <sup>b,f</sup>	70 ± 23 <sup>b</sup>	75 ± 20 <sup>f</sup>
(% of energy intake)	25.6 ± 1.7 <sup>b,d</sup>	27.1 ± 1.5 <sup>b</sup>	26.8 ± 1.8 <sup>d</sup>
Carbohydrate intake (g)	35 ± 8	40 ± 5	40 ± 5
(% of energy intake)	17.9 ± 4.6 <sup>d</sup>	16.6 ± 3.5	15.0 ± 3.3 <sup>d,*</sup>
Roast chicken	74 ± 55 <sup>d</sup>	80 ± 60	116 ± 46 <sup>d,**</sup>
Roast beef	72 ± 61	71 ± 57	90 ± 56
Salmon rolled in cheese	129 ± 54 <sup>a,e</sup>	199 ± 84 <sup>a</sup>	204 ± 65 <sup>e</sup>
Tuna and tomato salad	91 ± 40	100 ± 45	101 ± 42
Mayonnaise	94 ± 72 <sup>b,e</sup>	177 ± 101 <sup>b</sup>	196 ± 115 <sup>e</sup>
Cream of lentil soup	119 ± 57	135 ± 124	147 ± 102
Black cherries baked in batter	221 ± 63 <sup>c,f</sup>	257 ± 16 <sup>c</sup>	251 ± 33 <sup>f</sup>
Ratatouille	16 ± 4 <sup>a,d</sup>	9 ± 7 <sup>a</sup>	10 ± 7 <sup>d</sup>

2

3 All values are means ± SDs. Patients ate more protein from the buffet just after dialysis than  
4 they did on the interdialytic day, with no significant difference in energy content, fat and  
5 carbohydrate intake. The ratio of energy intake from protein to total energy intake was therefore  
6 higher after dialysis than it was on the interdialytic day, though it was similar for fat and lower  
7 for carbohydrates on the interdialytic day. In details (see supplemental material 3), compared  
8 with the interdialytic day, hemodialysis patients after dialysis ingested significantly more roast  
9 chicken and non-significantly (P=0.097), more roast beef, but similar amounts of the other

10 courses. \*, \*\* and \*\*\* indicate significant differences between the two days in hemodialysis  
11 patients with  $P < 0.05$ ,  $P < 0.01$  and  $P < 0.001$ , respectively. Healthy subjects differed from  
12 hemodialysis patients on the interdialytic day (results with the same letter indicate significant  
13 differences between those results, with a, b and c indicating  $P < 0.05$ ,  $P < 0.01$  and  $P < 0.001$ ,  
14 respectively) and the day after dialysis (d, e and f indicate  $P < 0.05$ ,  $P < 0.01$  and  $P < 0.001$ ,  
15 respectively).