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DISCOMFORT: NOT PAIN BUT STILL UNPLEASANT FEELINGS FROM THE GUT*

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Most of the factors initiating food or fluid intake have already been studied, but much less is known about those terminating ingestion. We have hypothetised that discomfort originating from the gastrointestinal system may be one of those factors. Gut distension cause pain if the intestinal volume changes but merely discomfort if only the tension of the gut wall increases. It seems that mild unpleasantness (i.e. discomfort) arising from the gut as a result of moderate (quasi-isometric) distension, among and in concordance with other factors, may significantly reduce intake and hence contribute to physiological satiety. The arising discomfort can be detected by measuring the amount and rate of the ingestion, by recording and analysing ingestive behavior by taste-aversivity and taste-reactivity tests, etc. Conclusions of all experiments point to the same direction: tension increase in the gut wall causes discomfort and results in decrease of intake, i.e. satiety.

Keywords: Gut discomfort – satiety – ingestion – taste-aversivity

INTRODUCTION

In his recently published unique monography, entitled "Visceral Perception" [1], *Ádám* described the visceral sensory procedure as being 'Janus-faced': in most of the time the observer or researcher faces difficulties to exactly detect visceral sensory events, though there is no question visceral perception is an existing phenomenon. As Ádám, using the terms coined by *Head* [19] puts it, the visceral afferent information usually remains in the *protopathic* range in which the perception – if at all exists – is diffuse, uncertain in space and time and does not represent a clear source. In agreement with many clinicians [15, 16, 21, 26, 27], he points out that visceral perception, as such, is a rare event usually associated with disordered or even pathological functioning; i.e. the *epicritic* range in this case is very narrow and the critical level is high [1]. On the other hand, it is clear that visceral afferent signals may and do influence behavior in a more-or-less direct way even if we do not have a con-

* Dedicated to Professor György Ádám on the occasion of his 80th birthday.

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scious account of that influence [e.g. 6, 15, 26, 27, 29]. The question, however, through what mechanisms the visceral influence on the behavior is realised has not yet been answered. In this paper we would like to suggest a mechanism which seems to work in this respect.

Our hypothesis was based on a general observation that visceral signals reaching consciousness were almost always unpleasant or even aversive in nature [1, 4, 15, 20, 24, 28]. This suggests that unpleasantness is somehow a part of the effect and may well be one of the factors that turns *protopathic* sensations into *epicritic* perception. The hypothesis examined here states that pain is not a necessary (though certainly sufficient) condition for the visceral signals to modify behavior, but a moderate unpleasantness, which we have termed as *discomfort* [6], is. The existence of such a category at all was first hypothetised after completing our earlier threshold and open-field experiments with intesinal distension [10, 12, 13] which proved that weak, mild, strong and painful visceral stimuli had differential effects on the ongoing behavior in rats. This structure of the afferent influence then has been studied in a series of animal experiments to test the hypothesis that mild unpleasantness, i.e. discomfort, is an inherent and possibly necessary condition for the visceral signals to directly influence behavior. In addition to these data, some evidence obtained in human studies supported our view which showed that in order to produce a visceral perception it is necessary – at least at the beginning – to reach the unpleasant range [1, 2, 3, 15, 22, 29]. In this paper we overview the evidences collected in our own studies that seem to prove the proposed 'discomfort' hypothesis.

MATERIALS AND METHODS

The model used was described several times in earlier publications [9, 13, 14]. The stimulated viscerosensory organ was the small intesine, namely the upper portion of the jejunum. In a few experiments, also the upper portion of the large intestine was used. In order to obtain a permanent surface for stimulation, a Thiry-Vella intestinal fistula was prepared, i.e. a portion of the gut was dissected with the blood- and nervous-supply intact and was sutured by both ends to the abdominal wall. This way a loop was formed, the musculature and skin over the loop was closed, thus only the orifices were open to outside. Since the normal passage was restored by parallel sutures, the rats had survived from a few month to even a year and a half. We were able to stimulate the hence formed loop without disturbing the feeding activity and without built-in chronic recording devices.

In the experiments overviewed here only mechanical stimulation was used: a balloon filled either with air or with water was placed into the loop. The two ways of stimulation differed significantly: the air filled ballon had only changed the tension of the gut wall since the air in the balloon could be compressed; whereas if the balloon was filled with water, no compression had occurred and the volume changed in proportion to the injected amount of fluid. We refer to the air-filled balloon as *isometric* (in fact quasi-isometric) stimulus whereas to the water-filled balloon as *volu-*

metric stimulus. For the volumetric stimulation, 0.05 ml, 0.09 ml, 0.12 ml or 0.28 ml volumes, respectively, were injected into the balloon, whereas for the isometric stimulation, the balloon was inflated by air pumped in until the pressure just overcame the resistence of the rubber.

In most of the experiments cited here we measured the fluid consumption of the rats deprived of water for 23.5 hours and usually simultaneously recorded the behavior of the animals. As described elsewhere [6, 11], recording was based on the fact that rats display a stereotype behavior when drinking: intensive consumption is followed by grooming, sniffing, orienting, searching for food and finally resting. If all these elements get a weight (from 1 to 6) and the time spent with the respective element is multiplied by this weight and the products are summed for each minute [6, 11], one creates a 'behavioral equivalent': a 'drinking equivalent', a 'grooming equivalent', an 'orienting equivalent', etc. We call this the *satiety index*. Similarly, aversive reactions can be classified according to the expected level of pain and discomfort: stamping, revolving, humping, twitching, withdrawal and jumping or vocalisation were the categories from the mildest to the most severe. To distinguish from the satiety index, negative weights were assigned, and the resulting behavioral equivalent was called *aversive index* [6, 7, 8]. If one computes these indices aganist the time, dynamics of the behavior can be followed in each session or in a series of sessions.

In a few rats the fistula was treated with the positive detergent benzalconium-chloride (BAC – Sigma, St. Louis, USA) before closing the wound. This detergent selectively ablated the myenteric plexus and disconnected afferent fibers from the receptors. In these rats effect of the volumetric distension on the free drinking was tested [23].

Taste-aversion and taste-reactivity tests were used to evaluate aversivity of the stimuli. Details of these studies were described elsewhere [8, 18]. In a special – yet unpublished – experiment we associated a new taste with the late phase of free drinking, i.e. with the state of satiety. In subsequent sessions both the taste presented earlier in the drinking phase or in the satiety phase, respectively, were tested in themselves for any taste-aversion effect.

RESULTS

Figure 1 shows the effect of volumetric stimulation on the free drinking behavior in the small intestine. Total intake gradually decreased as the stimulus volume increased. This decrease, however, could not be due to earlier satiety since the satiety indexes did not differ at all (Panel B). Aversive indexes, on the other hand, showed a gradual increase suggesting that some aversive effect was responsible for the reduction of drinking.

To prove that this unpleasant effect is principally mediated by the visceral afferents originating from the enteral nervous system (ENS), we treated the fistula with benzalkonium-chloride (BAC) which almost completely eliminated the aversive

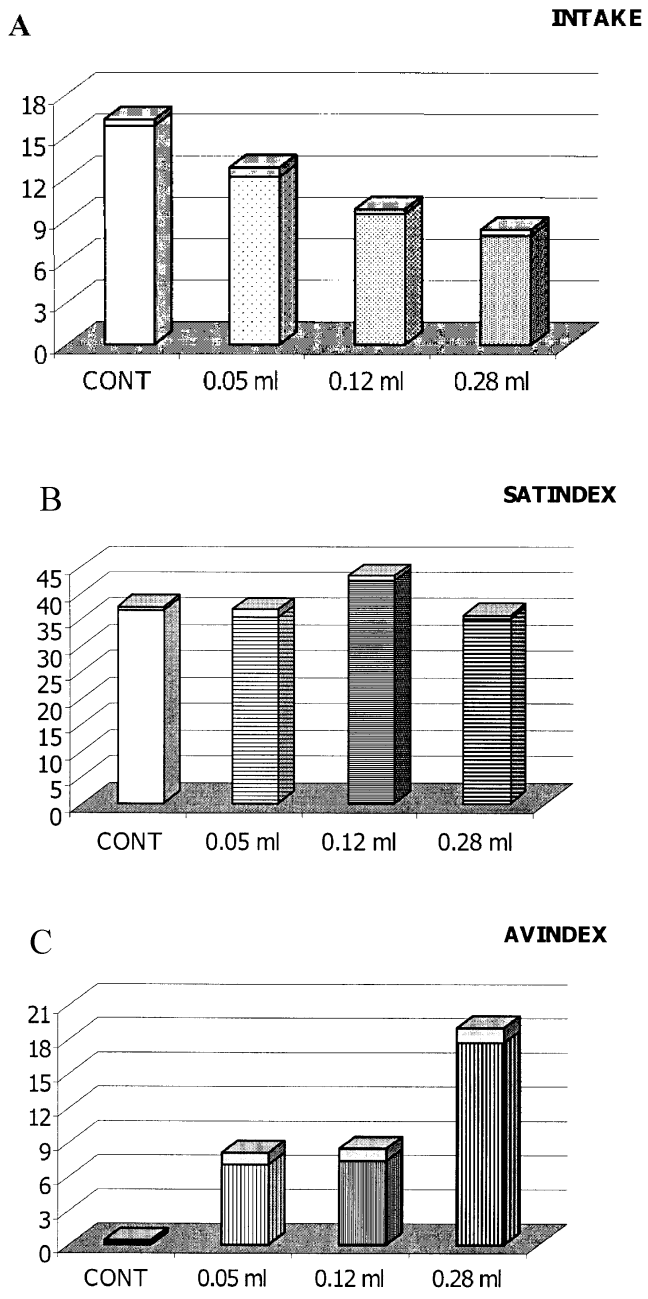

Fig. 1. Intake (A), satiety- (B) and aversive indexes (C) of 9 rats stimulated by volumetric distension (mean ±SE)

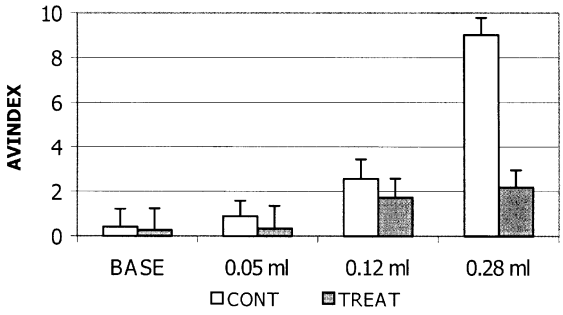

Fig. 2. Aversive indexes obtained with different volumetric stimuli in untreated (CONT) and BAC-treated (TREAT) rats

reactions (Fig. 2). We also found an interesting fact, namely that effects of 0.05 ml and 0.12 ml distension did not differ.

Figure 3 demonstrates the dynamics of the reduction of intake when isometric stimulus was given. Whereas the stimulation itself significantly reduced fluid intake, in the test phase intake was somewhat reduced but to a much less extent than in the stimulation phase. In other words, only moderate taste aversion occurred despite the fact that reduction of intake was similar to those obtained with volumetric distension.

Direct comparison of volumetric and isometric stimulation in the large intestinal fistula of 9 rats (Fig. 4) shows that despite the similarity of the ingested volume and the non-significant differences of the satiety indexes, aversive indexes differed significantly during stimulation (lower panel). In fact, this was the only significant difference between the two stimulus conditions.

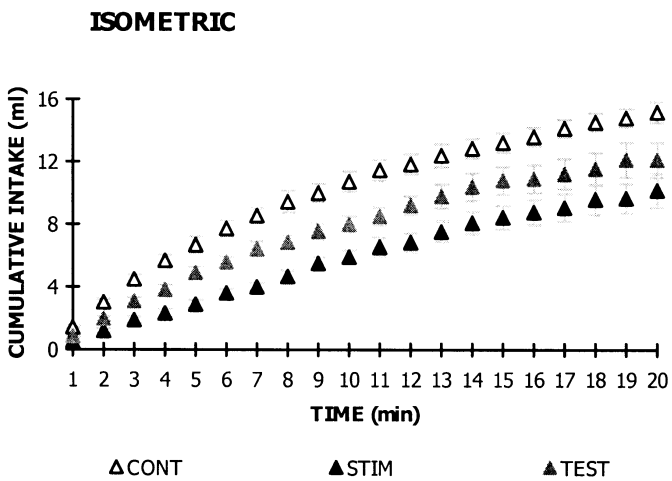

Fig. 3. A taste-aversion experiment demonstrating that learned aversion initiated by isometric distension is moderate (as compared to full aversion usually obtained with effective invasion)

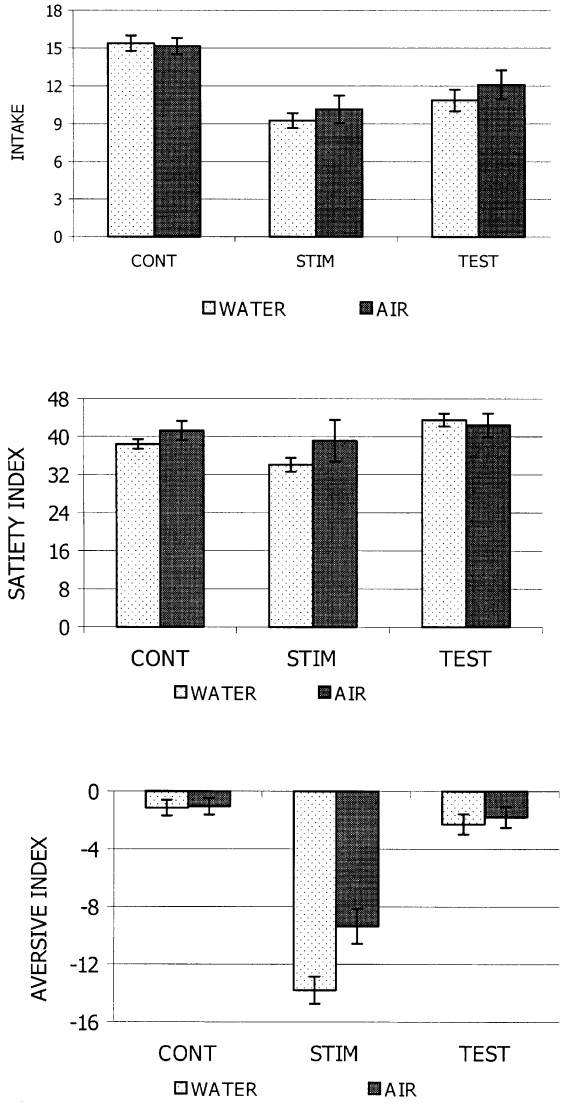

Fig. 4. Comparison of the effects of isometric (air) and volumetric (water) stimulation, respectively, to the intake (upper panel), satiety index (middle panel) and aversive index (lower panel) in the large intestine of the rat (mean±SE)

The taste-reactivity test yielded very interesting results (Fig. 5). Except in case of the 0.05 ml volume, aversive scores were low and similar to those obtained without stimulation. On the contrary, the number of consummative movements was significantly reduced when the rats were stimulated with 0.05 and 0.28 ml volume, respectively. Again, moderate volumes (0.09 ml and 0.12 ml) did not show this effect.

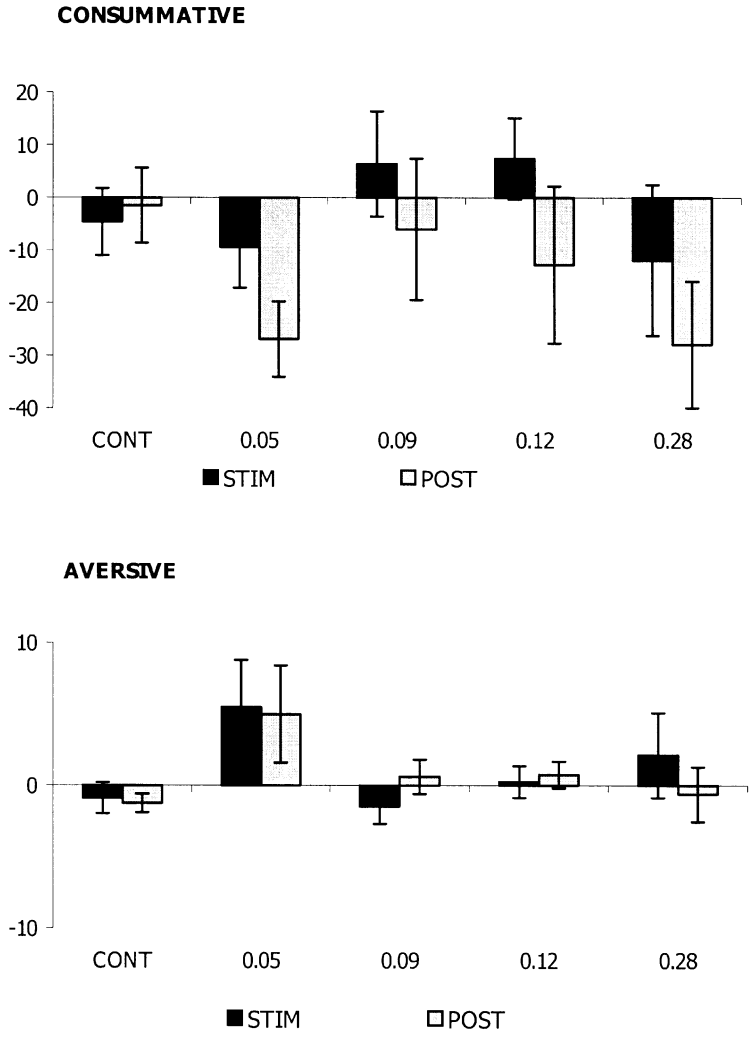

Fig. 5. Consummative (upper panel) and aversive (lower panel) responses of the rats in the taste reactivity test during and after stimulation as compared to the prestimulus baseline during volumetric stimulation with different intensities

Consummation scores were not only reduced during stimulation but – even more – in the post-stimulus period in case of and proportionally to all intensities.

In the last experiment reported here, a new taste was selectively associated with the last period of the free drinking sessions in which the rats showed the signs of satiety (Fig. 6). Subsequently, the base taste (water) or the associated taste (aroma) was solely given to the rats in consecutive experiments. As Figure 6 shows, rats con-

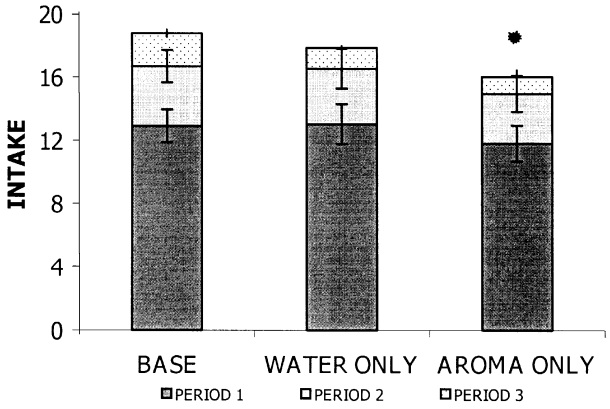

Fig. 6. Fluid consumption during the intensive (Period 1), intermediate (Period 2), and late (Period 3) phase in a free drinking experiment in which a new aroma taste was selectively associated with Period 3 (BASE). Intake in follow-up experiments in which water only or aroma only was given throughout the session are shown by the second and third bar, respectively. * denotes significant difference of the total intake

sumed significantly less from the aroma-flavoured fluid but not from the water. This reduction of intake is characteristic in all periods of the test session but most prominent in the first, intensive drinking phase.

DISCUSSION

All results point to the same direction: pain, though evidently being effective in this respect, is not necessary to reduce and terminate ingestive behavior, since much lower intensities seemed to be enough to reduce fluid intake of the rats or to elicite aversive learning. Low volume and isometric distension of the gut that cause mild discomfort (but clearly not pain) successfully reduced fluid consumption even in deprived rats. The fact that satiety indexes were not significantly different from those obtained in control sessions shows that the underlying mechanism is probably not an early satiety or an enhancement of satiety signals, but something else. The all-round increase of aversive scores during free drinking suggests that reduction of the intake is the consequence of some emerging discomfort. We believe this interpretation is further supported by the fact that a new taste associated with satiety itself acquired a negative character and resulted in a moderate taste-aversion.

The unexpected fact that the above-mentioned effects had not shown a monotonous increase as the stimulus volume increased deserves special attention. One might expect that if the gut volume increases the level of discomfort also increases. This was only true if the gut would behave in a steady way during distension. We suggest, however, that moderate distension activates a reflex relaxation which in turn decreases the strech of the gut wall and hence the consequent discomfort. Similar results

were obtained in human experiments in which the adaptation of the large intestine to distension was shown [30]. This, on one hand, supports the above hypothesis that volumetric distension may and can elicit discomfort, and on the other hand, proves that the resulting discomfort itself is the factor that reduces intake. Comparison of volumetric and isometric distension confirms this reasoning since isometric distension – at least under the circumstances of these experiments – had never caused pain but only discomfort though proved to be as effective in reducing intake as were volumetric stimuli. To sum it up, all our results are in line with the hypothesis outlined previously: discomfort might be an essential, or even a necessary condition for intake reduction during normal ingestive behavior.

If we now put together these results with *Ádám's* notion about the nature of visceral input, it seems plausible to suppose that it is the emotional-motivational character of the visceral signals that mediate their influence on the behavior. Thus, *discomfort* is rather a 'feeling' than a 'sensation', as was put forward by *Armstrong* in his early book on sensory processing [5] and therefore one might not expect any specific effects. This was proved by the lack of aversive elements in the taste-reactivity test and also by the fact we reported earlier that rats were unable to use gut distension stimuli as discriminative signals in operant conditioning [9]. On the other hand, pain has a strong discriminative power and can be used as a direct signal in learning procedure. These differences lead us to the suggestion that whereas pain usually signals damage or serious disorder of the intestinal system, discomfort is rather a tool to manage functional changes [7]. The idea just described is supported by the results of other authors, too [17, 25]

One might argue that usually a subject seldom consumes volumes large enough to reach the aversive range of satiety and thus to produce even a mild discomfort. This might certainly be true in adults (though men, due to the culturally mediated hedonic behavior, may be an exemption), it is probably not true in the youngs, especially in newborns. This is the time when individuals learn the signals that precede or are associated with the coming discomfort and this way learn how to moderate intake accordingly (i.e. to prevent unpleasant feelings from the gastrointestinal system). In other words, it is not necessary to have an *actual* discomfort but only the signs of its possibility – learned control helps to avoid it. Intermittent reinforcement of this learned control by occasional overeating or overdrinking might strengthen the control and may extend this learned phenomenon for longer periods.

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