Heartbeat and arrhythmia perception in diabetic autonomic neuropathy

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SYNOPSIS
A comparative study of diabetics with autonomic neuropathy (N = 13) as against non-neuropathic diabetics (N = 16) and healthy control persons (N = 20) was carried out with respect to heart rate both at rest and under stress, frequency of cardiac arrhythmias in a 24-h ECG and accuracy of heartbeat and arrhythmia perception. In the subjects with diabetic autonomic neuropathy, the spontaneous variability and stress-induced reactivity of the heart rate as well as the number of tachycardic episodes were reduced, whereas the frequency of ventricular extrasystoles was somewhat increased. Impaired heartbeat perception and a complete loss of perception of arrhythmias as a consequence of neuropathic deafferentation could be demonstrated. Cardiac perception disorders also play a vital role in other clinical problems, e.g. silent myocardial infarction and lack of awareness of hypoglycaemia in diabetes mellitus.

INTRODUCTION
Unpleasant bodily sensations play an important role in internal, psychosomatic and most psychiatric disorders. Distorted visceral perception in patients with panic disorders may trigger anxiety attacks (Ehlers et al. 1988a). Bodily complaints are an inevitable syndrome in depressive patients (DSM-III, APA, 1980; Kanfer & Hagerman, 1981). The diagnosis of internal diseases is likewise based on the subjective perception of physical symptoms.

For cardiac interoception, it has been demonstrated in laboratory studies that heartbeat perception in healthy subjects is influenced by gender (Whitehead et al. 1977; Jones & Hollandsworth, 1981), weight or body fat (Montgomery & Jones, 1984; Rouse et al. 1988), body position (Jones et al. 1987), physical activity (Jones & Hollandsworth, 1981), emotional arousal (Katzkin et al. 1982; Katkin, 1985) and emotionality (Schandry, 1981; Montgomery & Jones, 1982). However, it has also been found that less than 50% of the healthy population are reasonably good heartbeat perceivers (Schandry, 1981; Davis et al. 1986; Jones et al. 1987).

Considering that under most circumstances awareness of visceral sensations is of little relevance for healthy subjects, this appears plausible (cf. Jones et al. 1985). Nevertheless, most subjects can learn to discriminate their heartbeats (Brener & Jones, 1974; Davis et al. 1986; Jones et al. 1987).

Several clinical studies have endeavoured to determine whether patients with heart-related complaints or anxieties are more prone to perceiving their cardiac activity correctly. In laboratory studies it was found that patients with cardiac phobia (Stalmann et al. 1988), panic disorder (Ehlers et al. 1988b), hypochondriasis and anxiety neurosis (Tyrer et al. 1980) are somewhat more aware of their cardiac activity than healthy controls, whereas patients with mitral valve prolapse (Stalmann et al. 1988), specific phobia (Tyrer et al. 1980) or myocardial infarction (Jones et al. 1985) are not. But even the patients with increased cardiac awareness are not perfect in the perception of heartbeats, and only Ehlers et al. (1988b) reported a trend towards a higher percentage of panic patients classified as good cardiac perceivers.

Another approach to evaluating cardiac perceptivity has evolved from cardiology. The question of interest is whether there is a...
neuropathy was assessed with a heartbeat (mental) tracking task and an arrhythmia perception task. Whereas the latter is a natural and unobtrusive procedure for studying the perceptivity of arrhythmias, the validity and reliability of heartbeat (motor) tracking techniques are presumed to be low because the required motor responses interfere with the perceptual process (Pennebaker & Hoover, 1984). However, this is not the case for mental tracking. Secondly, the relationship among findings on all commonly used heartbeat perception tasks is weak (Jones et al. 1984; Pennebaker & Hoover, 1984; Davis et al. 1986), and so far there is no generally accepted method. Thirdly, and most importantly, the results of the mental tracking task employed are consistent with the findings on the arrhythmia perception task and, therefore, are very interesting in the context of the study as a whole.

The following three hypotheses were tested. (1) In patients with diabetic autonomic neuropathy, the spontaneous variability and the orthostatic reactivity of heart rate are diminished in comparison with patients with non-neuropathic diabetes mellitus and healthy control subjects. (2) The perception of heartbeat and autonomic neuropathy there is an increase in heart rate at rest and in the incidence of arrhythmias. (3) The perception of heartbeat is less accurate in patents with diabetic autonomic neuropathy than in the control groups. For patients with diabetic autonomic neuropathy, the spinal or sympathetic link is impaired. The spinal baroreflex arc may be less active in patients with diabetic autonomic neuropathy than in the control groups. Therefore, the cardiovascular and autonomic system can be affected in patients with diabetic autonomic neuropathy.

### METHOD

#### Subjects

Thirteen diabetics with autonomic neuropathy (DAN), 16 diabetics without neuropathy (DWN) and 20 healthy controls (HC) between 20 and 60 years of age were examined (Table 1).

<table>
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The electrocardiogram was recorded by means of two pre-cordial leads on C-120 tapes in a portable ECG-recorder (FM-Recorder MR-20).
that might facilitate the detection of heartbeats. The task was performed seven times to measure heartbeats and heart rate under various physical and psychological stress manipulations. The order of manipulation was as follows.

1. Supine 1 — after 10 min of relaxation in a supine position a perception interval of 30 s.

2. Supine 2 — immediately after getting up a perception interval of 25 s.

3. SITTING — after 5 min of relaxed sitting a perception interval of 25 s.

4. MENTAL STRESS — immediately after a 2-min subtraction task (starting with 1000, repeatedly subtracting 13) a perception interval of 30 s.

5. STANDING — immediately after imagining an anxiety-provoking situation for 2 min a perception interval of 30 s.

6. PHYSICAL EXERCISE — immediately after deep knee bends on one min a perception interval of 15 s.

7. Supine 2 — after 10 min of relaxation in a supine position a perception interval of 20 s.

At the end of each interval the subjects were requested to report how many heartbeats they had counted. Note that Schandry (1981) asked his subjects to report the number of heartbeats counted or estimated. We changed this instruction because we wanted the subjects to report the number of heartbeats (OB = objective beats) for the same interval. A perception score (PS) was calculated as follows (cf. Bentler et al., 1990):

\[ PS = 1 - \frac{OB}{SB} \]

Additionally, the responses were classified into three perception categories:

- exact perception: \( SB - OB \leq 2 \)
- poor perception: \( SB - OB > 2 \)
- no perception: \( SB = 0 \)

The perception score quantifies the accuracy of the perception of heartbeats on a continuous scale from 0 to 1, with a high score reflecting good perception. The perception categories 'exact perception' and 'no perception' represent the extremes. 'Exact perception' means that the subject was able to perceive all heartbeats in the perception interval. The deviation of \( 2 \) beats is tolerated because at the time of the time indicating onset or offset one beat can easily be missed or added (cf. Schandry, 1981). In contrast, 'no perception' reflects a total inability to perceive any heartbeats during the perception interval. Some subjects fell into this category because we asked the subjects to report the number of heartbeats counted, not estimated. Although there is no direct means of checking whether a subject's response is in fact based on the perception of discrete heartbeats, at least for the categories 'exact perception' and 'no perception' this seems to be the case. It is very unlikely that someone will achieve 'exact perception' without perceiving the actual heartbeats. Furthermore, there is no reason for a subject to report no heartbeats if he or she did in fact perceive heartbeats.

Heart rate perception

The subjects were instructed to mark all perceptions of irregular cardiac activity on the marker attached to the recorder. The 24-h ECGs were then examined for ventricular extrasystoles (VES), tachycardias (TACHY) and other cardiac irregularities. The arrhythmias were classified according to type and severity (Lown classification). Tachycardias were defined as an episode of increased heart rate that exceeded the baseline rate by 20% within 1 min. If a subject marked a cardiac perception up to 40 s after a ventricular extrasystole and 60 s after the commencement of a tachycardia this was considered an exact perception of an arrhythmia. The hit rate was defined as the ratio of exactly perceived arrhythmias (fEA) to the total number of arrhythmias (fA). The hit rate was calculated separately for ventricular arrhythmias (P-HIT-TACHY) and ventricular extrasystoles (P-HIT-YES):

\[ \text{hit rate: } (P\text{-HIT}) = \frac{f\text{(EA)}}{f\text{(A)}} \times 100\% \]

The error or 'false alarm' rate (P-FA) represents the proportion of events marked without preceding arrhythmia (f(M)) in relation to the total number of marks made (f(M)):

\[ \text{false alarm rate: } (P\text{-FA)} = \frac{f\text{(M)}}{f\text{(A)}} \times 100\% \]

hit and false alarm rates were calculated for each subject.

Statistical evaluation

Group differences were tested with a non-parametric test of significance (5%, two-tailed), if the Kruskal-Wallis rank variance analysis (H test) yielded significant group differences, then simultaneous post-hoc comparisons were made with the Newman-Keuls test. Changes in the heartbeat perception scores within the groups were tested with the Friedman rank variance analysis. The distribution of the two response categories 'exact perception' and 'no perception' was evaluated descriptively.

RESULTS

Heart rate

The diabetics with autonomic neuropathy tended to have the highest heart rate in the perception intervals (Fig. 1). Under physical stress (standing, physical exercise), however, these differences largely disappeared; this was because the increase in heart rate was more marked in the two control groups than in the group of diabetics with autonomic neuropathy. The difference in heart rate between the groups is significant only for the condition 'anxiety' (H test: \( P = 0.03 \); post-hoc comparisons: HC/DWN NS; HC/DAN \( P = 0.04 \); DWN/NS).

Spontaneous heart rate variability

Spontaneous heart rate fluctuation (R-R interval variation) was evaluated with a method proposed by Aizakixen et al. (1986). The evaluation is made at rest, whereby the difference between the shortest and longest interbeat interval within a period of 12 s is determined. The diabetics with autonomic neuropathy had a significantly lower spontaneous variation in heart rate than the non-neuropathic diabetics or the healthy controls (mean ± standard deviation; HC: 0.15 ± 0.06; DWN: 0.12 ± 0.05; DWN/NS). The diabetics with autonomic neuropathy had the worst overall perception scores, and this did not change within the test situations (Friedman test: \( P < 0.01 \)). They performed best in the anxiety condition and worst in the standing condition. The healthy control group achieved the best perception scores in all test conditions, with the poorest result in the sitting condition and the best in the anxiety condition (Friedman test: \( P = 0.05 \)). The differences between the groups are close to significance in the test conditions 'standing' (H test: \( P = 0.10 \), 'mental stress' (\( P = 0.12 \)), 'physical exercise' (\( P = 0.12 \)) and 'standing' (\( P = 0.08 \)). However, if the perception score is averaged across the two supine situations to stabilize the score, the group differences are significant (HC: 0.70 ± 0.19; DWN: 0.57 ± 0.23; DWN/NS; 0.40 ± 0.33; H test: \( P = 0.04 \); post-hoc comparisons: HC/DWN NS; HC/DAN \( P = 0.08 \); DWN/NS).
Similar results are revealed by the distribution of the two perception categories 'exact perception' and 'no perception' (Table 2). The healthy control group performed best, the diabetics with autonomic neuropathy worst. The relatively good performance of the healthy controls is reflected in the frequency of exact perceptions. Compared with both diabetic groups, more than twice as many of them were able to achieve an exact perception at least once (93% compared with 21 and 23%), and overall they had exact perceptions about twice as often as either diabetic group (14% compared with 6 and 9%). On the other hand, the impaired heartbeat perception ability of the diabetics with autonomic neuropathy is evident in the frequency of the 'no perception' responses. In all of the perception intervals they were unable to perceive any heartbeats, whereas this happened for the healthy controls and the diabetics without neuropathy in less than 10% of the intervals. Moreover, 31% of the diabetics with autonomic neuropathy were unable to perceive any heartbeats at all at least once, compared with only 17% of the healthy controls and 14% of the diabetics without neuropathy.

Examination of the results in the different heartbeat perception conditions reveals that the healthy controls performed best (see frequency of exact perceptions) in the situations 'anxiety', 'physical exercise' and 'supine II', and worst in the situations 'standing' and 'sitting'. The diabetics without neuropathy did not improve their frequency of exact perceptions in the situations where the healthy controls did. However, all of them were able to perceive at least some heartbeats in these situations, leading to a reduction in 'no perception' responses and an improvement in the perception score (see Fig. 2). The diabetics with autonomic neuropathy, on the other hand, were unable to improve their cardiac perception in the 'anxiety' and 'physical exercise' conditions. The frequency of intervals with imprecision of heartbeats did not change and, additionally, there were no intervals with exact perceptions.

**Frequency of arrhythmias**

On average, the diabetics with autonomic neuropathy had more ventricular extrasystoles and fewer tachycardias than the subjects in the two control groups (Fig. 3). While these differences are significant for tachycardias (H-test: P < 0.01; post-hoc comparisons: HC/DWN NS; HC/DAN P < 0.01; DWN/DAN P = 0.04) and ventricular extrasystoles (HC/DWN NS; HC/DAN P < 0.01), they are not significant for ventricular extrasystoles.

**Number of cardiac events marked**

Perceptions of cardiac activity were rare in all of the test groups. The mean number of events marked was 2.3 ± 4.2 in the control group, 1.6 ± 3.5 in the non-neuropathic diabetics and 0.15 ± 0.4 in the diabetics with autonomic neuropathy. The difference between the healthy controls and the diabetics with autonomic neuropathy is significant (H-test: P = 0.03; post-hoc comparisons: HC/DWN NS; HC/DAN P = 0.04; DWN/DAN NS).

**Perception of arrhythmias**

In the control group the hit rate was 13% ± 33% for ventricular extrasystoles and 5% ± 6% for tachycardias (Fig. 4). In the non-neuropathic diabetics, the hit rate for tachycardias was quite similar (4% ± 9%), whereas this group was unable to perceive ventricular extrasystoles correctly. The diabetics with autonomic neuropathy, on the other hand, were unable to perceive either tachycardias or ventricular extrasystoles. The group differences are significant for the tachycardia hit rate (H-test: P = 0.04; post-hoc comparisons: HC/DWN NS; HC/DAN P = 0.04; DWN/DAN NS), but not for the perception of ventricular extrasystoles.

The mean false alarm rate (P/F – FA) was 59% ± 40% in the control group, 57% ± 34% in the non-neuropathic diabetics and 100% ± 0% in the diabetics with neuropathy. However, the differences between the groups are not significant. **DISCUSSION**

In diabetics with autonomic neuropathy, the efficient and afferent innervation of the heart is disturbed. This leads to an alteration in cardiac activity and to disturbed perception of heartbeats and arrhythmias. Consistent with hypothesis 1, the diabetics with autonomic neuropathy had a reduced spontaneous variability of the inter-beat intervals, a lower orthostatic increase in heart rate, less frequent tachycardias and more frequent ventricular extrasystoles than the non-neuropathic diabetics or the healthy controls. An increased basal heart rate could be confirmed only as a tendency. Our findings were also consistent with the suppositions formulated in hypothesis 2. The healthy subjects achieved the best heartbeat perception scores in all test situations and the highest overall number of exact perceptions. As expected, they performed best in situations with psychological or physically induced arousal and worst in a standing or sitting position. The diabetics without neuropathy started out with relatively poor heartbeat perception, comparable to that of the diabetics with neuropathy; however, they were able to improve their performance markedly in the situations with arousal induction. This differentiated them clearly from the diabetics with autonomic neuropathy. The latter were unable to improve their heartbeat perception. Most characteristic for the diabetics with neuropathy was that many of them had a total...
imperception of heartbeats. Overall their perception of heartbeats was less accurate than that of the two control groups. Furthermore, consistent with hypothesis 3, the diabetics with autonomic neuropathy marked fewer cardiac events in the ambulatory 24-h ECG, and their cardiac sensations showed absolutely no connection with actual cardiac arrhythmias such as ventricular extrastoles and tachycardias. This total inability to perceive arrhythmias clearly differentiates the neuropathic diabetics from the healthy controls and in general from the non-neuropathic diabetics.

Our findings confirm that autonomic deafferentiation in diabetes mellitus leads to an impairment in the transmission of cardiac signals. In intact cardiac perceptivity, cardiac signals are decoded and processed in the ‘noise’ of the internal and external affereces, similar to external signals (Pennebaker, 1982). Autonomic deafferentiation reduces a translation in the cardiac signal rate, impairing the cardiac signal-to-noise ratio. Under ambulatory conditions (24-h ECG, arrhythmia perception task), i.e. normal noise level, the cardiac signal can no longer be perceived correctly, resulting in a total loss of arrhythmic perception. The conditions of the laboratory, on the other hand (heartbeat perception task, protection from external stimuli, concentration on the heart), reduce the general noise level and hence the signal-to-noise ratio artificially improved. Under such conditions, the effects of the autonomic neuropathy are somewhat less distinct, but still observable. Within the laboratory, the healthy controls and the diabetics without neuropathy achieved their best results in situations with arousal induction. Presumably, in these conditions the cardiac signal is strengthened by beta-adrenergic influences on the myocardium (Katkin, 1985). In diabetics with autonomic neuropathy the afferent transmission of the cardiac signal is impaired, and therefore these patients do not show a similar effect.

According to Brener (1974), perception and control of visceral activities could be transmitted via a central feedback pathway, an interoceptive afferent pathway and/or an interoceptive afferent pathway (cf. Jones et al. 1987). The confirmed impairment of cardiac perception due to neuropathic derangement of the heart suggests that cardiac perceptions are transmitted via visceral rather than sensory afferents. Moreover, peripheral neuropathy can be excluded because these patients did not reveal clinical signs of sensorimotor neuropathy and, additionally, cardiac neuropathy usually represents an early manifestation of diabetic nerve disorder (Clarke & Ewing, 1982).

Two methods, an arrhythmia perception task and a modified heartbeat tracking task, were used to assess cardiac perception. The arrhythmia perception task revealed unequivocal results, which clearly differentiated diabetics with autonomic neuropathy from the two control groups. This task seems to be a valid, clinically useful and naturalistic tool for evaluation of cardiac perceptivity. The additionally conducted modified tracking task basically confirmed the above findings. Therefore, in the context of the whole study, it is justifiable to report these results in spite of the recently questioned validity of the tracking method (Flynn & Clemens, 1988).

The cardiac perception deficiency as demonstrated in this study is clinically significant not only for perception of heartbeats and arrhythmias, but also for other cardiac affercnces. The loss of cardiac pain may lead to silent myocardial infarction, and the loss of hypoglycaemic awareness in diabetes mellitus even to hypoglycaemic coma. Additionally, the impaired visceral perception has indirect effects on the neuroendocrine and affective variables (Pauli et al. 1999).

This work was supported by grant no. Str 273/2-1 from the Deutsche Forschungsgemeinschaft.

REFERENCES


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