



## Fear of hypoglycemia in patients with type 2 diabetes: The role of interoceptive accuracy and prior episodes of hypoglycemia

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### ABSTRACT

**Objective:** Fear of hypoglycemia (FoH) is a limiting factor for diabetes self-management and can have detrimental effects on quality of life. However, relatively little is known about its underlying mechanisms. In line with findings on patients with anxiety disorders, we hypothesized that interoceptive accuracy (IA) might be positively linked to FoH in patients with type 2 diabetes (T2DM).

**Methods:** 133 patients with T2DM were screened according to the extreme quartiles of the Hypoglycemia Fear Survey worry subscale (HFS-W). Overall, 66 participants (HFS-W < 4; HFS-W > 17) were included in the present study. Participants completed questionnaires on sociodemographic and diabetes-related measures. Accuracy of heartbeat perception was assessed using the mental tracking task.

**Results:** Contrary to expectations, IA did not differ significantly between patients with low and high FoH. A linear regression analysis demonstrated that the experience of mild hypoglycemia ( $\beta = 0.32, p \leq 0.01$ ) and its interaction with IA ( $\beta = -0.26, p = 0.040$ ) were significant predictors of FoH, indicating that low IA and a history of experiencing mild hypoglycemia are positively associated with FoH.

**Conclusion:** Our findings suggest a positive association of low IA in combination with prior episodes of hypoglycemia and FoH in patients with T2DM. The results are in line with recent findings on IA in patients with chronic somatic symptom distress more generally and contribute to our understanding of the relations between interoception, body related fears, and physical symptom perception.

### 1. Introduction

Hypoglycemic events are a limiting factor for glycemic control [1] and can have detrimental effects on psychosocial outcomes such as decreased well-being [2,3] and quality of life [4–7]. Furthermore, hypoglycemic events can increase diabetes related distress, depression [8,9] and mortality [10]. In turn, adverse psychosocial outcomes are known to impair self-management. Hence, these may result in a vicious circle of unstable glycemic control and more frequent hypoglycemic events [11,12].

Aversive aspects of hypoglycemic episodes, such as unpleasant symptoms and worrisome consequences, may lead to the development of fear of hypoglycemia (FoH) in some patients [1,5]. FoH often promotes dysfunctional behavior in order to avoid hypoglycemia; for

example, keeping blood glucose levels high by limiting physical activity, reducing the required insulin dose, or excessive consumption of carbohydrates. This maladaptive behavior of patients suffering from FoH may lead to more frequent and/or persistent hyperglycemia and increases the risk of micro- and macro-vascular complications [13]. The majority of available literature, however, has focused primarily on T1DM and relatively little is known about the underlying mechanisms of FoH in T2DM. However, recent studies suggest that FoH and elevated worries in regard with hypoglycemia as well as avoidance behaviors associated with FoH are not uncommon in people with T2DM, even in those who do not use insulin [14–16]. It is conceivable that patients with T1DM and those with T2DM may differ in the experience of FoH, given, for example, the relatively limited exposure to (severe) hypoglycemia in patients with T2DM compared to T1DM. Thus, there may

**Abbreviations:** BMI, body mass index; BPM, beats per minute; FoH, fear of hypoglycemia; HFS-R, Hypoglycemia Fear Survey; IA, interoceptive accuracy; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus

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**Table 1**

Sociodemographic and diabetes-related baseline information as well as performance scores on the mental tracking task (means and standard deviations in parentheses) for the low FoH group and the high FoH group.

	Low FoH group (n = 33)	High FoH group (n = 33)	Statistics (df)	p	Effect size
Age [years]	58.42 (10.25)	57.70 (7.88)	0.32 (64)	0.75	0.05
Female n (%)	15 (45.45)	20 (60.61)	1.52 (1)	0.32	0.15
BMI [kg/m <sup>2</sup> ]	33.24 (7.64)	32.64 (6.27)	0.35 (64)	0.73	0.06
Diabetes duration [years]	10.26 (6.46)	9.97 (8.43)	0.16 (64)	0.88	0.03
Baseline heart rate [bpm]	73.68 (16.35)	74.61 (12.59)	−0.26 (64)	0.80	0.04
HbA <sub>1c</sub> [%]	7.62 (1.45)	7.82 (1.70)	−0.52 (63)	0.61	0.08
Insulin-treated n (%)	22 (66.67)	28 (84.85)	2.97 (1)	0.15	0.21
Episodes of mild hypoglycemia in the previous 6 months	0.41 (0.71)	1.00 (1.02)	−2.65** (60)	0.01	0.45
Episodes of severe hypoglycemia in the previous 6 months	≤ 0.01 (≤ 0.01)	0.06 (0.25)	−1.44 (63)	0.15	0.24
Interoceptive accuracy	0.31 (0.26)	0.39 (0.31)	−1.05 (64)	0.30	0.18

Note. Independent sample *t*-tests were calculated for continuous variables, with Cohen's *d* as an effect size estimate, and the chi-square procedure was applied for dichotomous variables, reporting *w* as an effect size estimate. BMI = body mass index; bpm = beats per minute.

IA was measured by the performance score on the mental tracking task.

\*\*  $p \leq 0.01$ .

be other important factors that contribute to the development and maintenance of FoH in people with T2DM.

Several person-level factors have been found to contribute to the development and maintenance of FoH: For instance, demographic (e.g. female gender), psychological (e.g. state and trait anxiety) and diabetes-specific factors, such as intensified insulin therapy and particularly the experience of severe hypoglycemic events [17–20].

We propose that FoH may also be linked to increased interoceptive accuracy (IA) [21], the sensitivity to accurately assess bodily sensations [22]. A number of emotion theories assume that arousal plays a vital role in the formation of emotions. As noted by Schachter in the two-factor theory of emotion, the cognitive label largely determines the quality of emotion, but “emotionality is positively related to physiological arousal” (p. 65) [23]. Thus, arousal determines the intensity of the emotional experience and individuals with enhanced IA report more intense emotional experiences due to their increased perception of this arousal [24].

There has been numerous research on the effects of IA on anxiety. Enhanced IA has been positively related to state [25] and trait anxiety [26–30], and to clinical anxiety [28,31,32]. It is well known that patients with increased anxiety sensitivity and anxiety disorders generally report hypervigilance for somatic sensations in self-report measures [12,33–35]. High IA may result in an increased perception of body symptoms, stronger allocation of attentional resources to bodily sensations, and changes in physiological arousal. Further, patients with clinical anxieties do not only self-report an increased perception of somatic sensations, they also seem to have a subsequent dysfunctional cognitive appraisal of these sensations biased towards a catastrophizing interpretational style [36–38].

For insulin-using patients with diabetes, it is of utter importance to recognize their typical symptoms of low blood sugar levels early to be able to counteract hypoglycemia quickly. However, early symptoms of hypoglycemia and anxiety-related symptoms can highly overlap (e.g. trembling, sweating) and thus may be difficult to discriminate [39]. Hence, one can assume that patients with diabetes are more likely to interpret these bodily changes in a catastrophizing (e.g. upcoming hypoglycemic event) and danger-related way—even in cases of minor and normal body sensations. The interpretation of perceived body signals as dangerous may further shift attention towards these signals and enhances physical sensations themselves in a positive feedback loop [40]. Repeated threatening interpretations of even normal body sensations may—in the long-run—lead to a conditioned anxiety response to interoceptive cues, which is believed to play a pivotal role in the maintenance of anxieties [41].

Due to the scarce empirical evidence of underlying mechanisms of FoH in T2DM, the primary aim of the study was to better understand the role of IA as a potentially contributing component for the

development of FoH. In line with findings on IA in patients with anxiety disorders (especially panic disorder), we hypothesized that IA would be positively associated to FoH in patients with T2DM.

## 2. Method

### 2.1. Participants

The sample consisted of 133 patients with T2DM, who were recruited in seven large diabetes outpatient care centers to participate in a previous FoH study (Klostermann et al., unpublished manuscript) and were screened according to the extreme quartiles of the Hypoglycemia Fear Survey worry subscale sum score (HFS-W) [42,43].

Overall, we included 33 participants with low FoH (first quartile, HFS-W < 4) and 33 participants with high FoH (fourth quartile, HFS-W > 16) in the present study. Participants were invited for an experimental session to assess their IA. All participants were insulin treated or used oral anti-diabetic medication. Low and High FoH groups did not differ with respect to sex, age, heart rate, body mass index, diabetes duration, HbA<sub>1c</sub>-score, episodes of mild and severe hypoglycemia (past 6 months), or insulin therapy (Table 1). The study was approved by the local ethics committee of the Department of Psychology at the Johannes Gutenberg- University of Mainz. All participants provided written informed consent prior to participation.

## 3. Measures and procedure

### 3.1. Self-report data

All participants completed a screening questionnaire regarding sociodemographic and diabetes-related information (e.g. diabetes duration, long-term complications etc.) and a German version of the HFS-R [42,43], which was professionally translated and has been used in other studies before [44,45].

The HFS-R is a self-report questionnaire consisting of two subscales (worry and behavior) with 23 items rated on a five-point Likert scale (0 = never – 4 = always). In the present study, only the worry subscale (HFS-W) was used for analyses. This scale includes 13 items assessing emotional concerns about various aspects of hypoglycemia and its negative consequences, HFS-W sum score of the first quartile was < 4 (low FoH group), whereas HFS-W sum score of the fourth quartile was > 16 (high FoH group). In the present sample Cronbach's  $\alpha$  for the HFS-W was  $\alpha = 0.96$ .

### 3.2. Heartbeat assessment

An electrocardiogram was obtained by attaching three Ag-AgCl

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