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Characteristics influencing expected cognitive performance during hypoglycaemia in type 2 diabetes

J.Z. Petersen[a,b], M. Nilsson[c], J. Rungby[c,d], K.W. Miskowiak[a,b,*]

[a] Psychiatric Centre Copenhagen, Copenhagen University Hospital, Rigshospitalet Dep. 6233, Blegdamsvej 9, DK-2100, Copenhagen, Denmark
[b] Department of Psychology, University of Copenhagen, Øster Farimagsgade 2A, DK-1353, Copenhagen, Denmark
[c] Bispebjerg University Hospital, Department of Endocrinology, Copenhagen, Denmark
[d] Copenhagen Center for Translational Research, Bispebjerg University Hospital, Copenhagen, Denmark

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ABSTRACT

Background: Acute hypoglycaemia is associated with cognitive impairment in patients with type 2 diabetes. However, there is limited understanding of the relationship between patients' expected cognitive difficulties and their objectively-measured deficits during non-severe hypoglycaemia.
Objective: This report investigates demographic and clinical factors associated with the discrepancy between expected (i.e., self-evaluated) and measurable (i.e., neuropsychological) cognitive functions in patients with type 2 diabetes during acute non-severe hypoglycaemia.
Methods: We performed an analysis of factors associated with the relationship between expected and measurable cognitive performance for data collected from a cohort of patients with type 2 diabetes (N = 25). Patients attended two experimental visits during which we performed hyper-insulinaemic glucose clamping; (i) non-severe hypoglycaemic clamp (plasma glucose (PG): 3.1 ± 0.3 mmol/L) and (ii) normoglycaemic clamp (PG: 5.8 ± 0.3 mmol/L), as part of a double-blinded cross-over study. During hypoglycaemia, patients' expected cognitive performance was assessed with a visual analogue scale after which objective cognitive functions were assessed with a neuropsychological test battery. We computed a global 'cognitive discrepancy' composite variable with score values on a scale between -10 and +10 using a novel statistical formula that creates a discrepancy score between subjective and objective cognition. Positive values reflect more expected than objectively-measured difficulties, while negative values reflect disproportionately more objectively-measured than expected cognitive difficulties. We used paired samples *t*-tests to compare degree of cognitive discrepancy between conditions of hypo- and normoglycaemia, while multiple regression analysis was performed to identify factors associated with the degree and direction of the cognitive discrepancy. The significance level for the analyses was $p \leq 0.05$ (two-tailed).
Results: Patients generally underestimated their cognitive abilities (M = 1.6, SD = 3.3) during hypoglycaemia compared to normoglycaemia (M = −1.0, SD = 3.5) ($p = 0.2$), t(23) = 2.9, $p < 0.01$. Underestimation of cognitive capacity during hypoglycaemia was more pronounced for patients with younger age (β = 0.5, $p = 0.02$), higher verbal IQ (β = 0.5, $p = 0.03$), and more hypoglycaemia-related shakiness (β = 0.4, $p = 0.03$).
Limitations: The modest sample size limits the generalizability of the findings.
Conclusions: Patients with type 2 diabetes underestimated their cognitive abilities during non-severe hypoglycaemic states, especially those with younger age, higher IQ, and more hypoglycaemia-related shakiness. These patients may thus have excessive preoccupations with their cognitive difficulties in relation to cognitively challenging daily life situations.

1. Introduction

Hypoglycaemia (plasma glucose (PG) levels ≤3.9 mmol/L) is a key clinical feature in patients with type 2 diabetes (prevalence rate 6–45%) (Cryer, 2002; Edridge et al., 2015). Acute hypoglycaemia results in decline of cognitive functioning (Allen et al., 2015; Feinkohl et al., 2014; Graveling et al., 2013; Nilsson et al., 2019) that may endure immediately after normoglycaemic restoration (Zammitt et al., 2008).

* Corresponding author at: Psychiatric Centre Copenhagen, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.
E-mail addresses: jeff.zarp.petersen@regionh.dk (J.Z. Petersen), malin.sofia.desiree.nilsson@regionh.dk (M. Nilsson), jr@biomed.au.dk (J. Rungby), kamilla.miskowiak@regionh.dk (K.W. Miskowiak).

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This cognitive deterioration is likely caused by altered brain glucose metabolism (Rooijackers et al., 2016) as evidenced by need for recruitment of greater neural resources to maintain cognitive performance during hypoglycaemia (Bolo et al., 2011; Gejl et al., 2018). In daily life, intact cognitive functioning is important for activities such as planning, organizing, and decision making. Therefore, hypoglycaemia can impair patients' daily functioning and has been associated with increased risk of traumatic injuries, including car accidents (Signorovitch et al., 2013). Such potential consequences may fuel patients' fear of hypoglycaemia and associated sudden cognitive decline in daily life (Wild et al., 2007). However, due to interindividual variation in the PG levels at which cognition is affected (Rooijackers et al., 2016), the glycaemic threshold at which patients experience cognitive deterioration varies between patients. Therefore, insight into the relation between patients' *subjectively* experienced cognitive capacity and *objectively* measured cognitive performance during hypoglycaemic states may guide future clinical assessments of cognitive impairment during hypoglycaemia.

It is well-established that people's subjective estimations of their own cognitive abilities do not necessarily reflect their actual objectively measured performance on neuropsychological tests. Indeed, a poor relationship between subjective and objective cognition has been observed across neuropsychiatric disorders and healthy populations (Miskowiak et al., 2016; Petersen et al., 2019; Stenfors et al., 2013). However, there is limited understanding of the relationship between *expected* (i.e., subjectively-evaluated) and *measurable* (i.e., neuropsychological) cognitive difficulties in patients with type 2 diabetes during hypoglycaemia. This needs to be further addressed to understand whether patients evaluate their cognitive abilities realistically before deciding to engage in cognitively challenging daily life activities (e.g., driving). Specifically, identification of factors associated with discrepancy between subjective and objective cognition (i.e., over- or under-estimation of cognitive capacity) may guide future clinical assessments of cognition in this patient group and may help inform patients about the extent of their cognitive impairments during hypoglycaemic conditions and how they may be tackled.

This report analyses the data from a recent study of the effects of non-severe hypoglycaemia on cognition in diabetes type 2 patients (Nilsson et al., 2019). Here, we aim to quantify the degree and direction of potential discrepancy between expected and measured cognitive impairment during acute insulin-induced hypoglycaemia (target PG 3 mmol/L [54 mg/dl]) in patients with type 2 diabetes. Specifically, we aim to explore demographic and clinical factors associated with this potential cognitive discrepancy.

2. Materials and methods

2.1. Study design

This analysis is based on data from a randomised, double-blinded, cross-over study of patients with type 2 diabetes (Nilsson et al., 2019), which involved comparison of cognitive performance from two experimental visits of hyperinsulinaemic glucose clamping; (i) hypoglycaemic clamp (aiming for a PG target of 3.0 ± 0.2 mmol/L) and (ii) normoglycaemic clamp (PG clamp target 6.0 ± 0.2 mmol/L) were performed on separate occasions. We separated the two experimental visits by 21–42 days to avoid potential effects of counter-regulatory hormone responses or other physiological effects of hypoglycaemia.

2.2. Participants

Included participants were diagnosed with type 2 diabetes for at least 3 months. Eligible patients met the inclusion criteria for type 2 diabetes treated with diet or antidiabetic medication (except sulfonylureas or insulin), 35–70 years of age, a BMI between 23–35 kg/m^2, and haemoglobin A1c (HbA1c) below 75 mmol/mol. Patients were excluded if they had severe diabetic complications, recent ischemic cardiac disease or other major illnesses. Full inclusion and exclusion criteria are listed in Supplementary Table 1. We determined randomization by sequential enrolment and lowest available number assignment. Patients were blinded to the sequence of glycaemic conditions and to their current blood glucose concentration. All participants provided oral and written consent before participation. The study was designed and performed in accordance with the Helsinki Declaration of Good Clinical Practise, approved by the local ethics committee, and was registered at www.clinicaltrials.gov (NCT03014011).

2.3. Procedures

Patients attended the research unit at the Department of Endocrinology, Bispebjerg University Hospital, following an overnight fast, having refrained from strenuous physical exercise and alcohol three days before. A cannula was inserted in an antecubital vein for blood sampling and the arm was kept heated throughout the examination to arterialize venous blood. A second cannula was inserted into an antecubital vein in the contralateral arm for continuous infusion of glucose (20%) and human soluble insulin (Actrapid, Novo Nordisk, Bagsværd, Denmark). After a 15-minute baseline period, a 3-minute priming regimen was started and thereafter insulin was infused at a constant rate of 100 mU x m^{-2} x min^{-1}, which was kept stable during neurocognitive testing. A variable infusion of glucose was given simultaneously and adjusted to maintain target glucose levels. Blood sampling for glucose was made at 5-minute intervals throughout the clamp procedure. Plasma glucose was measured by the glucose oxidase method, using a glucose analyser (Yellow Springs Instrument, YSI Inc., Yellow Springs, OH). Neurocognitive testing was initiated when glucose levels had been stable for 40 min. After the neuropsychological assessment, the participants were served a meal and glucose levels were monitored until normoglycaemia was safely maintained.

2.4. Measures of objective and subjective cognition

Objective measures of cognition consisted of neuropsychological tests from a test battery assessing the following domains: attention and psychomotor speed, verbal learning and memory, and executive functions. The test battery included the Rey Auditory Verbal Learning Test (RAVLT) (Miskowiak et al., 2008; Schmidt, 1996), Trail Making Test Part A and B (TMT-A, TMT-B) (Army Individual Test Battery, 1944), Symbol Digit Modalities Test (SDMT) (Randolph et al., 1998), Wechsler Adult Intelligence Scale 3rd edition Letter-Number Sequencing Test (WAIS-III LNS) (Wechsler, 1997), Verbal Fluency Test (VFL; with letters 'S' and 'D') (Borkowski et al., 1967), and the Rapid Visual Information Processing (RVP) subtest from the Cambridge Automated Neuropsychological Test Battery (CANTAB). Verbal intelligence quotient (IQ) was assessed with the Danish Adult Reading Test (DART) (Crawford et al., 1987). We did not assess the impact of potential test-retest effect between the two experimental visits due to the randomized cross-over design of the study, which ensured that the participants received neuropsychological assessment in counter-balanced order. However, we used alternate versions of the objective, neuropsychological tests associated with the greatest learning effects (RAVLT, SDMT) to reduce potential learning effects between the two experimental visits.

Patients' subjectively-expected cognitive performance was evaluated with a visual analogue scale (VAS) completed at each visit (i.e., during normoglycaemia and hypoglycaemia, respectively) just prior to the objective neuropsychological assessment. On this scale, patients had to indicate how they expected to perform (on the VAS ranging from lowest to highest performance level) on tests of memory, attention, and concentration based on their present physical state. The total duration of the neurocognitive assessment at each visit was approximately 45 min and was conducted by a blinded research assistant from the

Table 1
Demographic and clinical characteristics of patients.

N	25
Gender, female/male, n (%)	10/15 (40/60)
Age, mean ± SD	60 ± 7
BMI, kg/m^2, M ± SD	30.5 ± 3.4
HbA1c, mmol/mol, M ± SD	53.6 ± 9.4
HbA1c, %, M ± SD	7.1 ± 0.9
Duration of diabetes in years, M ± SD	6.2 ± 3.7
Number of diabetic medications, M	1.6
Number of medications, M ± SD	5.1 ± 2.4
Years of education, M ± SD	13.6 ± 2.9
DART score, M ± SD	33.6 ± 8.8
Vital signs at screening visit	
Systolic blood pressure, mmHg, M ± SD	133 ± 12
Diastolic blood pressure, mmHg, M ± SD	79 ± 7
Heart rate, beats/min, M ± SD	70 ± 14
Reported hypoglycaemic symptoms during the clamp procedure	
None, no. (%)	5 (20%)
Sweating/sensation of warmth, no. (%)	15 (60%)
Fatigue, no. (%)	10 (40%)
Shakiness, no. (%)	7 (28%)
Rapid heartbeat, no. (%)	3 (12%)
Cold feet, no. (%)	1 (4%)
Dry mouth, no. (%)	1 (4%)
Stomach ache, no. (%)	1 (4%)

M = mean; SD = standard deviations; DART = Danish Adult Reading Test; HbA1c = Hemoglobin A1c (glycated hemoglobin); mmHg = millimetre of mercury.

NEAD Group, Psychiatric Centre, Copenhagen, Rigshospitalet (www.neadgroup.org).

2.5. Measures of hypoglycaemia-related symptoms

On each experimental visit, patients were informed of the characteristic symptoms of hypoglycaemia (stated in the Edinburgh Hypoglycaemia Scale; Deary et al., 1993) and instructed to inform the investigator of any hypoglycaemia-related symptoms occurring during the clamp procedure (Table 1).

2.6. Statistical procedures

2.6.1. Cognitive sensitivity score computation

We implemented a statistical methodology from our previous analyses (Miskowiak et al., 2016; Petersen et al., 2019) to derive 'cognitive sensitivity scores' that reflect the degree and direction of discrepancy between patients' subjective expectations to cognitive difficulties reported on the self-rating VAS and their objective impairment on the neuropsychological tests. The 'cognitive sensitivity scores' rely on the assumption that complete accordance of insight into one's cognitive functioning would result in the same rank ordering between subjective perceptions and objective performance level (presuming that these are valid measures of the same construct). We compute?). Accordingly, a sensitivity score of +10 indicates maximum 'sensitivity', with patients expecting the worst performance on objective neuropsychological tests, while a sensitivity score of -10 indicates maximum 'stoicism' with patients performing the worst on neuropsychological tests, despite expecting least cognitive difficulties. A value of 0 represents complete accordance between patients' expectation and objectively-measured cognitive functioning (i.e., the worst expectations in patients with marked objective decrease, and no decrease in those who do not expect any difficulties).

Specifically, we computed a global 'cognitive sensitivity score' by *z*-transforming raw scores from the neuropsychological tests and patients' expected cognitive performance reported on the VAS scale. *z*-scores were calculated from the mean and standard deviation (SD) values of these cognitive measures from the patient group. We reversed score values of the TMT-A and TMT-B (Army Individual Test Battery, 1944) and the RVP latency measure (i.e., higher raw scores on these measures received lower *z*-scores) to ensure equal directionality of the *z*-scores across objective and subjective cognitive performance scores. The individual *z*-scores for each cognitive measure were averaged into a global objective and a global subjective 'cognitive sensitivity composite' *z*-score, respectively. These 'cognitive sensitivity composite' *z*-scores were then converted into re-scaled scores (with values ranging from 0 to 10) using the following equation:

Equation 1. Formula used to derive 'cognitive sensitivity' scores

$$Re - scale\,formula = \left(\frac{(new_{max} - new_{min})}{(old_{max} - old_{min})} * (x - old_{max})\right) + new_{max}$$

In this equation, 'x' represents each individual patient's composite *z*-score. 'old_{min}' and 'old_{max}' comprise the lowest and highest values of the *original* *z*-scores on the global objective composite and the global subjective composite, respectively. 'new_{min}' and 'new_{max}' represent the *new* minimum and maximum scores (converted into re-scaled score values from 0 to 10). Finally, cognitive sensitivity scores were calculated by subtracting the re-scaled subjective composite score (based on the subjective VAS item scores) from the equivalent re-scaled objective composite score (based on the neuropsychological test item scores) resulting in values between -10 and +10.

2.7. Data analysis

All statistical analyses were conducted using the *Statistical Package for the Social Sciences* (SPSS version 25, IBM Corporation, Armonk, NY). We applied the Shapiro-Wilk test (Shapiro and Wilk, 1965) to assess whether data deviated from the normal distribution. Paired samples *t*-test was used to compare the degree of expected cognitive difficulties with objectively-measured impairments during hypoglycaemia and normoglycaemia, respectively. We performed a multiple linear regression analysis using the 'Enter' method to identify factors associated with the discrepancy between expected and measurable cognitive functioning during hypoglycaemia. The selection of variables was informed by the characteristics that had a significant impact on the degree and direction of discrepancy between subjective and objective cognition in our previous studies including patients with mood disorders (Miskowiak et al., 2016; Petersen et al., 2019). Due to the small sample size of the present study, we decided a priori to include only the following variables in the interest of maintaining statistical power: age, verbal IQ, illness duration (diabetes duration in years) as well as the following subjectively-reported hypoglycaemia-related symptoms: sweating and shakiness. The significance level for the analyses was $p \leq 0.05$ (two-tailed). *p*-values were not corrected for multiple comparisons due to the exploratory nature of this analysis.

3. Results

3.1. Patient characteristics and normality of data

A total of 37 patients with type 2 diabetes were screened between May 2017 and July 2018, of whom 28 were randomized and 25 completed both experimental visits. Patients' age mean was 60 ± 7 years (range 46–69 years), BMI 30.5 ± 3.4 kg/m2, and their HbA1c 53.6 ± 9.4 mmol/mol. The duration of their diabetes at the time of inclusion was 6 ± 4 years (Table 1). A stable glucose plateau was achieved during each condition. Mean PG concentration during the neurocognitive tests was 3.13 ± 0.27 mmol/L for the hypoglycaemic clamp and 5.83 ± 0.31 mmol/L for the normoglycaemic clamp. 80% of patients reported symptoms related to hypoglycaemia (Table 1) to the investigator on the day of the hypoglycaemic clamp visit. The three major physical complaints reported included sweating/sensation of warmth (63%), fatigue (42%), and shakiness (30%) (Table 1).

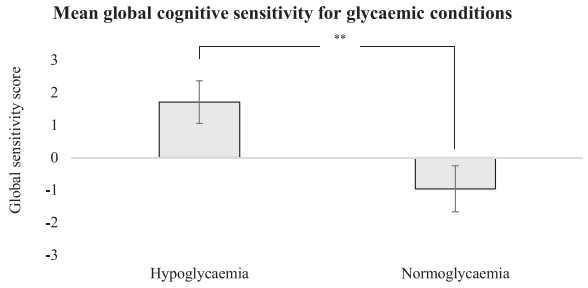

Fig. 1. A paired samples *t*-test comparing the mean global composite cognitive sensitivity scores for hypoglycaemia and normoglycaemia conditions revealed substantially greater expectation of cognitive decline during hypoglycaemia than normoglycaemia in patients with type 2 diabetes. Bars represent means. Error bars represent standard errors of the means. $^{**}p < 0.01$.

Data for the global composite cognitive sensitivity scores for hypoglycaemia and normoglycaemia conditions, respectively, were normally distributed (Shapiro-Wilk test, *p-values* ≥ 0.1).

3.2. Cognitive composite discrepancy between expected and actual cognitive performance

During the hypoglycaemic clamp visit, 79% of patients (n = 19) underestimated their cognitive functioning, which was reduced to 42% (n = 10) at the normoglycaemic clamp visit. Patients underestimated their cognitive abilities (M = 1.7, SD = 3.3) to a larger extent during hypoglycaemia ($p < 0.05$) compared to normoglycaemia (M = −1.0, SD = 3.5) with a greater accordance between expected and actual cognitive performance ($p = 0.2$), t(23) = 2.9, $p < 0.01$, Cohen's $d = 0.8$ (Fig. 1).

3.3. Factors associated with underestimation of cognitive capacity

The multiple linear regression model, including the global composite cognitive sensitivity score as the dependent variable, was statistically significant, F(5,19) = 3.6, $p < 0.05$, adj. $R^2 = 0.4$ with the following variables being associated with greater expected than measurable cognitive difficulties during the hypoglycaemic clamp: Younger age (standardized Beta (std. β) = 0.5, $p < 0.05$) (Fig. 2a), higher verbal IQ (std. β = 0.5, $p < 0.05$) (Fig. 2b), and presence of subjectively-reported hypoglycaemia-related shakiness (std. β = 0.4, $p < 0.05$) (for remaining variables: *p*-values ≥ 0.06). The regression model, including the global composite cognitive sensitivity score for the normoglycaemic clamp, was not significant ($p = 0.5$).

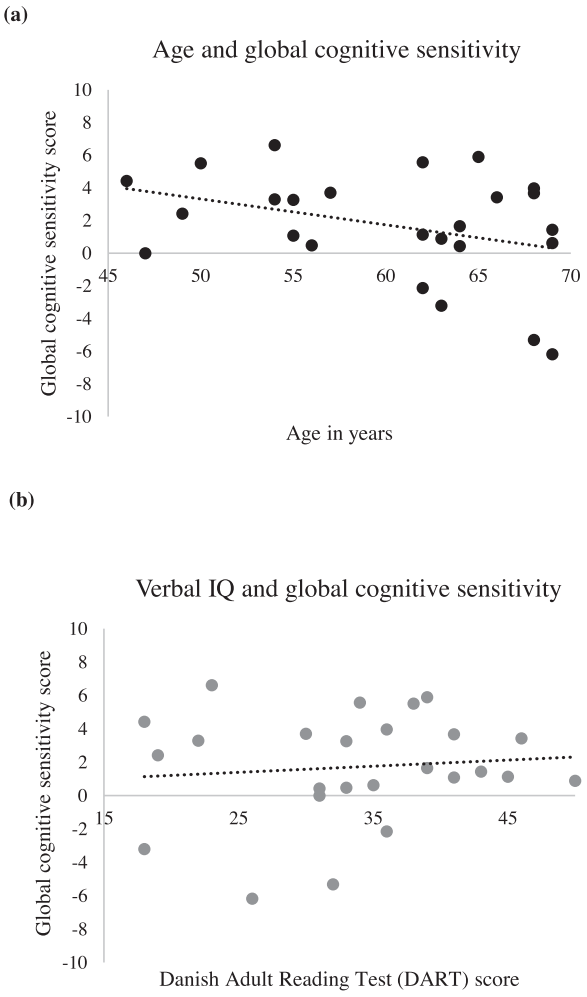

Fig. 2. (a) Relationship between age and degree of expected cognitive difficulties (global cognitive composite sensitivity score) during hypoglycaemia in patients with type 2 diabetes. The black dotted line shows a negative linear relation between increasing age and global sensitivity score, indicating that younger age is associated with greater expected than measurable cognitive impairment, while advancing age is associated with reduced expectation of cognitive impairment. (b) Relationship between verbal IQ and degree of expected cognitive difficulties (global cognitive composite sensitivity score) during hypoglycaemia in patients with type 2 diabetes. The black dotted line reveals a positive linear relation between verbal IQ and global sensitivity score, indicating that higher intelligence is associated with greater expected than measurable cognitive impairment.

4. Discussion

This study quantified the degree and direction of discrepancy between expected and measurable cognitive functioning during hypoglycaemia and examined characteristics related to this discrepancy in patients with type 2 diabetes. Overall, we found that patients were relatively accurate in estimating their cognitive functioning during normoglycaemia but underestimated their cognitive capacity during hypoglycaemia. Specifically, the majority (~80%) displayed disproportionately greater expected than measurable cognitive decline during hypoglycaemia compared to normoglycaemia (~40%). Hypoglycaemia thus led patients to underestimate their cognitive capacity. This was particularly pronounced for those with younger age, higher premorbid IQ, and more hypoglycaemia-related shakiness.

Our demonstration of a poor relationship between patients' subjective and objective cognition during hypoglycaemia corroborates previous detections of a similar cognitive disparity in other patient groups (Gelonch et al., 2017; Miskowiak et al., 2016; Petersen et al., 2019; Zamarian et al., 2015) as well as between perceived and measured disability across other domains, including mouth dryness, fall risk, and neck disability (Bezzina et al., 2017; Delbaere et al., 2010; Schmitt et al., 2009). Indeed, accumulating evidence points to a central role of negative bias on the tendency toward overestimating disability and the risk of poor outcomes (Farrin et al., 2003; Miskowiak et al., 2016). This suggests that the subjective-objective discrepancy is a general phenomenon that does not only pertain to cognition and is influenced by negative bias in patients' perception of their present and future difficulties.

The association between a higher degree of underestimation of cognitive functions and younger age is in line with prior findings of more prevalent cognitive complaints in younger compared with older patients with major depressive disorder (Bortolato et al., 2014; Petersen et al., 2019; Srisurapanont et al., 2015). A partial explanation for this association could be that younger patients are more likely employed or under education at the time of assessments. In keeping with this interpretation, the age range in the sample of the present study was 46–69

years. It is conceivable that younger patients are exposed to more situations with cognitively demanding tasks in their daily life that require full functional capacity. Cognitive decline may thus be particularly disabling for these patients, as it impedes their ability to maintain functioning in educational and vocational settings. Another explanation could be that older patients with longer illness duration have more insight into their cognitive capacity during hypoglycaemic episodes than newly diagnosed patients. In fact, our findings seem to suggest that there may be potential tendency towards overestimation of cognitive capacity in patients > 65 years of age (cf., Fig. 2a). However, this is hypothesis-generating evidence based on a small number of participants, which needs to be further addressed in future studies before firm conclusions can be drawn.

The relation between premorbid verbal IQ and expected cognitive difficulties is consistent with recent findings of a correlation between intelligence and self-evaluated cognitive functioning in depressed patients (Serra-Blasco et al., 2019). This could suggest that even subtle cognitive decrease is experienced as a major deterioration for high-functioning individuals with supra-normal premorbid functioning. On the other hand, the association could also reflect a more accurate sense of cognitive abilities in those who experience a decline from their usual performance level that is not captured by neuropsychological tests. Interestingly, the finding contrasts with our previous detection of a relation between higher verbal IQ and fewer subjective than objective cognitive impairments in bipolar disorder (Miskowiak et al., 2016). Thus, it cannot be excluded that a higher premorbid functioning level may also provide better strategies to compensate for the clinical manifestation of cognitive impairment (resulting in a tendency to under-report deficits). Taken together, the role of premorbid functioning on subjectively-perceived cognitive impairment may be versatile and warrants further investigation in diabetes.

Finally, the association between more hypoglycaemia-related shakiness and greater underestimation of cognitive capacity is consistent with evidence from other patient groups. The worse patients feel (e.g., in terms of lower quality of life and more stress), the greater the underestimation of their functions (Bezzina et al., 2017; Delbaere et al., 2010; Miskowiak et al., 2016; Petersen et al., 2019). This relation is consistent with cognitive theories assuming that physical and psychological discomfort may introduce a negative cognitive bias that leads to underestimation of functioning across domains (Beck, 1979; Bower, 1981). In daily life, patients may thus overestimate their cognitive impairment when they are mildly hypoglycaemic and therefore be less likely to get into a car and drive - particularly if they are "shaky". This is important given our recent finding that non-severe hypoglycaemia reduces psychomotor speed, working memory and sustained attention that are all crucial for safe driving (Nilsson et al., 2019).

There are various clinical implications of the finding that patients with younger age, higher verbal IQ, and more subjectively-perceived hypoglycaemia symptoms are more likely to underestimate their cognitive abilities during hypoglycaemia. Since these patients seem to be excessively preoccupied with hypoglycaemia-related cognitive impairments, they may also be especially overcautious in engaging in cognitively challenging daily situations (such as driving a car). This highlights the importance of assessing both subjective and objective cognitive functioning in patients with type 2 diabetes during hypoglycaemic conditions. Indeed, it seems especially warranted to perform a neuropsychological screening in younger, high-functioning patients with considerable hypoglycaemia symptoms to clarify whether they have objectively-verified impairments during hypoglycaemia. This would allow for initiation of cognitive compensation strategies in those with objective impairments, who should also be advised not to drive, during hypoglycaemia. Moreover, those who do not present with cognitive decline during hypoglycaemia should be recommended being less cautious of engaging in cognitively challenging activities in daily life. In addition, future studies with larger sample sizes should ideally explore the degree of discrepancy within individual cognitive domains to enhance insight into patients' appraisal of specific cognitive functions during hypoglycaemia. This would allow for more targeted recommendations on how to tackle specific cognitive impairments during hypoglycaemic conditions.

A strength of this report was the application of a novel statistical methodology to explore demographic and clinical factors associated with the discrepancy between subjective and objective cognitive functioning during hypoglycaemia. A limitation was that the *z*-score calculations of cognitive data were based on means and SDs from the patient group itself and not on data from a healthy control population. In addition, the modest sample size is a limitation of the present report, since this reduces the generalizability of the results and could have led to type II errors in the assessment of factors influencing the discrepancy between subjective and objective cognition. The present findings should therefore be considered hypothesis-generating and larger studies are warranted before any firm conclusions can be drawn regarding the characteristics influencing expected cognitive performance during hypoglycaemia. Accordingly, the small sample size did not allow us to investigate the potential impact of metabolic measures on the degree and direction of cognitive sensitivity. Taken together, our findings should therefore be regarded as preliminary and hypothesis-generating and require replication in future studies with larger sample sizes.

5. Conclusion

This report provides new insight into characteristics influencing the discrepancy between expected and measured cognitive decline during acute non-severe hypoglycaemia in patients with type 2 diabetes. The findings suggest that patients generally underestimate their cognitive difficulties during hypoglycaemia. Patients who are young, have high IQ and experience more hypoglycaemia symptoms seem to have greater expected than measurable cognitive decline during hypoglycaemia.

Declaration of Competing Interest

KWM has received consultancy fees from Janssen and Allergan in the past three years. JZP, JR and MN report no financial interests or potential conflicts of interest pertaining to this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.104431.

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