ORIGINAL RESEARCH

Disruption in time projection and non-adherence to long-term therapies

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Objective: Patients' non-adherence to medical prescriptions is a crucial issue in contemporary medicine because it can jeopardize care efficacy. Non-adherence is especially frequent in patients with chronic diseases. In this article, we propose that a particular condition, which we call disruption in time projection, is a cause of non-adherence to medication therapies in chronic diseases.

Methods: A questionnaire was administered to 120 hospitalized people with type 2 diabetes addressing three psychological constructs defining time projection: patience/impatience in a fictive monetary scenario (preferring to receive €1,500 in 1 year or €500 today), magnitude of temporal horizon (greater or lesser ability to imagine future events) and perception of the degree of physical similarity of current self to self at 1 year, 5 years and 10 years from the present. In addition, the questionnaire evaluated adherence to medication, social deprivation and depression.

Results: In the multivariate analyses, two factors were associated with adherence to medication: patience ($P<0.001$) and long temporal horizon ($P=0.006$). Two factors were associated with HbA1c $\geq 8\%$ (64 mmol/mol): non-adherence to medication ($P=0.003$) and short temporal horizon ($P=0.011$). Three factors were associated with long temporal horizon: adherence to medication ($P<0.001$), patience ($P<0.001$) and the existence of grandchildren ($P=0.002$). Social deprivation ($P<0.001$), non-adherence ($P<0.001$), female gender ($P=0.002$) and short temporal horizon ($P=0.050$) were associated with impatience. Finally, an association of adherence to expected similarity in the future to current self, impatience, short temporal horizon, social deprivation and depression was also shown in a multiple correspondence analysis.

Conclusion: What we termed a disruption in time projection may be a unique determinant for non-adherence to long-term therapy and, therefore, may influence the outcome of chronic diseases. We hypothesize that this is involved in both intentional and unintentional non-adherence and that it represents the loss of a protective mechanism. If this novel concept is to be confirmed in other settings and generalized to other chronic diseases, the recognition of its role in disease prognosis may help orient the teaching and practice of medicine.

Keywords: adherence, temporal horizon, impatience, disruption in time projection, social deprivation, depression, type 2 diabetes, chronic diseases

Introduction

Non-adherence to medication occurs frequently and can jeopardize the efficacy of long-term therapies. In people with diabetes, it is associated with reduced effectiveness of medications on HbA1c,[1] higher risks of complications, increased rates of hospitalization, greater health care costs and higher mortality.[2,3] Thus, non-adherence is a crucial issue for contemporary medicine:[4] Haynes, quoted by the WHO, stated that "Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment".[4]

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In general, it is believed that non-adherence to medication is driven by patient factors, type of therapy (complexity and side effects), quality of the patient–physician relationship[5–7] and the overall health care system.[4] However, one characteristic of non-adherence has been less attended to so far: non-adherence to long-term therapies concerns *chronic* diseases specifically, which form the largest part of the burden of health care at present. This suggests that the patients' relationship to temporality may be key to understanding the basic mechanisms of adherence: if the choice between adherent and non-adherent behavior is driven by the attractiveness of their respective rewards, it can be expected that a significant number of patients will choose non-adherence, whose reward is immediate and concrete, while the reward for adherence (avoiding complications) is abstract and remote.[8] Consistent with this idea, non-adherence has been found to be more frequent in younger people, for whom the prospect of living with the disease may entail a longer time duration.[9] Non-adherence is also more frequent in socially deprived patients,[10] whose most immediate priorities may not include their health status. Thus, we hypothesized that being adherent is associated with giving priority to the future.[11,12]

Therefore, this work tested the hypothesis that adherence to medication in chronic diseases is linked to time projection, defined herein as consisting of three psychological constructs: patience/impatience, size of temporal horizon (greater or lesser ability to imagine remote future events) and perception of the degree of physical similarity of current self to future self. This study was performed on people with type 2 diabetes; therefore, in addition, we investigated the connection between time projection and HbA1c levels.

Research design and methods

This study included a sample of 120 people with type 2 diabetes (65 men and 55 women), who were hospitalized, either for diabetic complications or for insufficient diabetes control, at a university hospital in the north suburb of Paris. Terminal kidney failure was an exclusion criterion. The study period lasted from May 19, 2016 to February 21, 2017. Recruitment continued until the final sample size of the study (n=120) was reached; this was intended to be larger than that of a previous study (n=80) describing the association between the temporal horizon and smoking habits.[13] The study was approved in April 2016 by an Ethical Review Board (Comité Consultatif sur le Traitement de l'Information en matière de Recherche Scientifique, C.C.T.I.R.S.). All patients received a document explaining the study and indicating that they were free to accept or refuse filling up the questionnaire, and gave their written informed consent for their participation.

To prevent missing data, the questionnaire was administered in the presence of a resident (YB) who explained the questions if needed. The questionnaire included the following categories. 1) Demographic data: gender, age, time since diagnosis of diabetes (referred to below as diabetes duration), marital status and existence of children and grandchildren, employment status, body mass index (BMI), last documented HbA1c level, smoking status and the presence of complications of diabetes. 2) Adherence to medication, assessed using the French six-item validated Girerd questionnaire, with questions such as "Do you think that you have too many tablets to take?" People were considered non-adherent if the number of positive responses to the items was ≥3.[14] 3) Impatience, determined using a simple fictive monetary scenario: if you are offered €500 today or €1,500 1 year from now, what would you choose?[15] 4) Temporal horizon, judged using two methods:[13] first, patients were asked to list five events that would happen to them and indicate their expected age when they occurred; the temporal horizon (in years) was determined as the difference between age at the final event and the patient's current age. Second, they were asked to complete the following story- "Joe, drinking his coffee, starts to think of the future. He thinks that" – and give the duration of the end they had imagined. 5) The degree of physical similarity of one's present self to the future self was determined by asking patients how they imagined they would look like physically, in comparison to today, in 1 month, 1 year, 5 years and 10 years.[16] 6) Social deprivation was measured using the 11-item EPICES questionnaire, with scores >30 indicating social deprivation.[17] Finally, depression was assessed with the 13-item (short-form) Beck Depression Inventory questionnaire, with scores greater than four indicating depression.[18] The complete questionnaire had 45 items and can be obtained from the main author by request. Questions asked to the patients to collect their demographic data and to address time projection are to be found in Figure A1. The Girerd questionnaire (adherence), EPICES (social deprivation) and the Beck questionnaire (depression) can be found elsewhere.[14,17,18] Finally, we used the two first questions of the 13-item depression Beck's questionnaire to indicate pessimism and sadness, respectively.

Data analyses

The primary outcome was adherence to medication. The results were dichotomised into adherent (<3 positive answers to the Girerd questionnaire) and non-adherent (≥3).[14] Logistic regression was performed to evaluate associations with patient characteristics. HbA1c was dichotomised into <8 or ≥8% (8%=64 mmol/mol), indicating acceptable or poor metabolic control in these hospitalized patients and logistic regression was used to calculate the determinants

of HbA1c. The determinants of temporal horizon and impatience were analyzed using negative binomial regression and logistic regression, respectively. Repeated-measures ANOVA were used to perform the comparison of the evolution of the degree of similarity over time between adherent and non-adherent patients. Finally, a multiple correspondence analysis (MCA) was performed, using the parameters selected from the previous results: HbA1c ($<8/\geq8\%$, $<64/\geq64$ mmol/mol), age ($<60/\geq60$ years old), diabetes duration ($\leq10/10-20/>20$ years), grandchildren (yes/no), impatience/patience in the monetary choice, smoking status (never/quit/active), temporal horizon ($\leq1/2-5/>5$ years), treatment adherence/non-adherence ($0-2/\geq3$ positive answer), physical self-similarity at 10 years ($>50/\leq50\%$), social deprivation (yes/no), depression (yes/no) and pessimistic/non-pessimistic and sad (yes/no) answers in the depression questionnaire. Euclidean distances and Ward's method were used to perform unsupervised hierarchical clustering on all the dimensions of the MCA. Clusters were defined by cutting branches off the dendrogram.

There were no missing data. All the tests were two-sided at a significance level of $P<0.05$. R statistical software version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria) was used to conduct the analyses.

Results
Demographical and psychological data
In all, 120 patients were included in the study. Recruitment was limited only by refusal to participate or inability to read and write or understand the questionnaire, either due to a linguistic barrier or limited literacy, as is frequently met with in this hospital. The mean age of the patients was 58.6±8.9 years old and the mean diabetes duration was 14.5±8.9 years. A mean BMI of 29.0±5.4 kg/m² was found, and their mean HbA1c levels were 9.8%±2.4% (84±14.5 mmol/mol). In all, 90.8% of the patients had children and 47.5% had grandchildren. Of the total, 44.2% never smoked, 27.5% were active smokers and 27.5% had quit smoking.

Table 1 presents the complete demographic description of the patients.

Table 2 presents the results of the psychosocial questionnaires. Only one-third of the patients gave fewer than three positive answers to the Girerd questionnaire, which would be consistent with adherent status. One-third gave the patient answer to the monetary choice question (preferring waiting 1 year for €1,500), half were socially deprived and one-third showed signs of depression, sadness and pessimism. The median temporal horizon was found to be 2.5 years for the event-determination method and 30 days for the story determination method. The degree of expected physical similarity of the future to the current self decreased progressively over time, reaching 43.3% at 10 years, but with large standard deviations.

Determinants of adherence to medication
In the univariate analysis (the results of which are given in Table 3), the following characteristics were associated with adherence to medication (defined as fewer than three

Table 1 Demographic description of the sample population

Characteristics	Median	Q1:Q3		
Age (years)	59	(53:67)		
Diabetes duration	14	(8:21)		
HbA1c (%) (mmol/mol)	9.2 (77)	(8.3:11.0) (67.2:96.7)		
BMI (kg/m²)	28.9	(25.6:32.4)		
Gender	**Female**			
N (%)	55 (45.8%)			
Marital status	**Married**	**Living as a couple**	**Divorced**	**Widow/er**
N (%)	70 (58.3%)	8 (6.7%)	13 (10.8%)	13 (10.8%)
Children	109 (90.8%)			
Grandchildren	57 (47.5%)			
Professional activity	**Unstable**	**No employment**	**In search of employment**	**Disability**
N (%)	12 (10%)	79 (58.3%)	5 (4.2%)	7 (5.8%)
Treatment	**OAD**	**OAD + insulin**	**Basal bolus**	
N (%)	32 (26.7%)	23 (19.2%)	65 (54.2%)	
Smoking habits	**Quit**	**Active**	**Never**	
N (%)	33 (27.5%)	34 (27.5%)	53 (44.2%)	
Complications	**Stent**	**Neuropathy**	**Retinopathy**	
N (%)	16 (13.3%)	68 (56.7%)	57 (47.5%)	

Note: Bold figures represent statistically significant.
Abbreviations: BMI, body mass index; OAD, oral antidiabetic drug.

Table 2 Answers to the psychological questionnaires

Characteristics	Value
Adherence (Girerd questionnaire)	
Number of positive answers, median (Q1:Q3)	3 (1:4)
<3 positive answers (adherent), n (%)	47 (39.2%)
Impatience/patience (monetary choice), n (%)	
Prefer €500 now (impatient)	76 (63.3%)
Prefer €1,500 in a year (patient)	44 (36.7%)
Temporal horizon	
Events method (years), median (Q1:Q3)	2.5 (1:5)
Story method (days), median (Q1:Q3)	30 (2:3,650)
Similarity to current self, mean ± SD	
1 month	97.3±10
1 year	87.8±13.1
5 years	67.4±23.2
10 years	43.3±30.5
Social deprivation (EPICES questionnaire)	
Score, median (Q1:Q3)	28.7 (21.9:51.5)
Socially deprived (score >30), n (%)	55 (45.8%)
Depression (Beck Depression Inventory)	
Score, median (Q1:Q3)	2 (0:5)
Depressed (score >4), n (%)	43 (35.8%)
Not sad, n (%)	82 (68.3%)
Not pessimistic, n (%)	35 (29.2%)

Note: Sad and pessimistic are assessed using the answers to the two first questions in the Beck Depression Inventory.

positive answers in the Girerd questionnaire): long temporal horizon, as determined by the event method (OR, 1.24; 95% CI, 1.11–1.38; $P<0.001$), impatient answer for the monetary choice question (OR, 0.11; 95% CI, 0.05–0.26; $P<0.001$), HbA1c ≥8% (64 mmol/mol) (OR, 0.02; 95% CI, 0.01–0.18; $P<0.001$), depression (OR, 0.22; 95% CI, 0.09–0.054; $P<0.001$), social deprivation (OR, 0.39; 95% CI 0.18–0.83; $P=0.015$) and age ≥60 years old (OR, 2.11; 95% CI, 1.00–4.45; $P=0.050$). In addition, we observed that the degree of expected physical similarity with the current aspect at 1 year, 5 years and 10 years was higher in adherent people (Figure 1); however, this trend did not reach statistical significance ($P=0.09$).

In multivariate analysis, using all these variables with the exception of HbA1c, two factors only were found to be significantly associated with adherence to medication: impatience (OR, 0.20; 95% CI, 0.08–0.51; $P=0.006$) and long temporal horizon (OR, 1.17; 95% CI 1.05–1.31; $P=0.006$). When temporal horizon was excluded from multivariate analysis, two determinants were found associated with adherence: impatience (OR, 0.14; 95% CI, 0.06–0.35; $P<0.001$) and depression (OR, 0.38; 95% CI 0.14–1.02;

Table 3 Univariate analysis of adherence (Girerd questionnaire)

Characteristics	Category	OR (95% CI)	P-value
Age (years)	≥60	2.11 (1.00–4.45)	**0.050**
HbA1c	≥8% (64 mmol/mol)	0.02 (0.01–0.18)	**<0.001**
Temporal horizon (events method)		1.24 (1.11–1.38)	**<0.001**
Social deprivation (EPICES questionnaire)	Score >30	0.39 (0.18–0.83)	**0.015**
Patience/impatience in monetary choice	Impatient	0.11 (0.05–0.26)	**<0.001**
Depression (Beck Depression Inventory)	Score >4	0.22 (0.09–0.54)	**<0.001**
Gender	Female	1.41 (0.68–2.95)	0.36
Activity	Stable	0.63 (0.25–1.59)	0.32
Marital status	Couple	0.92 (0.43–1.98)	0.83
Children	Yes	1.14 (0.31–4.13)	0.84
Grandchildren	Yes	1.1 (0.53–2.29)	0.80
BMI	>24	1.09 (0.43–2.75)	0.85
Smoking status	Quit	1.00	
	Never	0.73 (0.3–1.76)	0.48
	Active	0.65 (0.25–1.75)	0.40
Diabetes duration (years)		1.02 (0.98–1.06)	0.32
Retinopathy	Yes	0.96 (0.46–1.99)	0.90
Neuropathy	Yes	1.4 (0.67–2.96)	0.37
Stent	Yes	1.67 (0.58–4.8)	0.34
Treatment	Basal insulin	0.94 (0.45–1.96)	0.86
Similarity at 1 year (%)		1.01 (0.98–1.04)	0.59
At 5 years		1.01 (0.99–1.03)	0.29
At 10 years		1.01 (1.00–1.02)	**0.064**
Sad (Beck Depression Inventory)	Yes	0.52 (0.23–1.19)	0.12
Pessimistic (Beck Depression Inventory)	Yes	0.52 (0.22–1.21)	0.13

Note: Bold figures represent statistically significant.
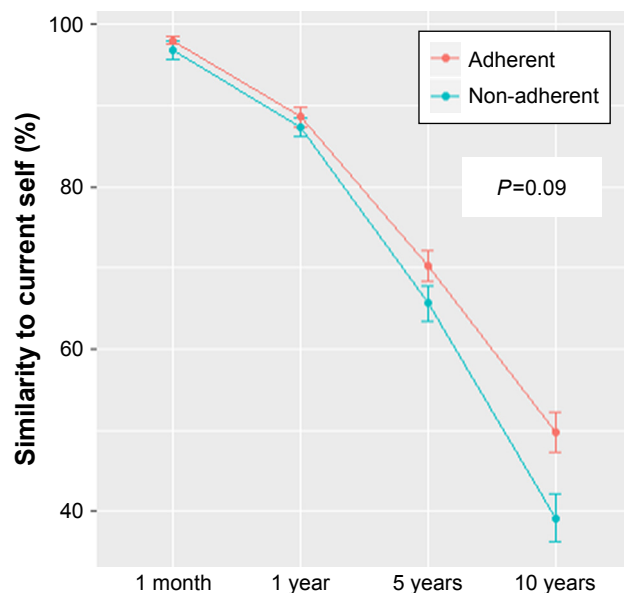**Abbreviation:** BMI, body mass index.

Figure 1 Evolution of the degree of similarity over time in adherent and non-adherent patients.
Notes: Physical similarity to current self: patients were asked how they thought that they would resemble their current physical aspect in 1 month, 1 year, 5 years and 10 years from now and to indicate the % of similarity. Mean ± SEM is indicated. Repeated-measures ANOVA were used to perform the comparison of data observed in the adherent and non-adherent patients.
Abbreviation: SEM, standard error of the mean.

P=0.055). When impatience was excluded from the multivariate analysis, two factors were found to be associated with adherence: long temporal horizon (OR, 1.20; 95% CI, 1.08–1.34; P<0.001) and depression (OR, 0.37; 95% CI, 0.14–0.96; P=0.041). Figure 2 shows ROC curves for these three models, yielding AUC values of 0.81 (95% CI,
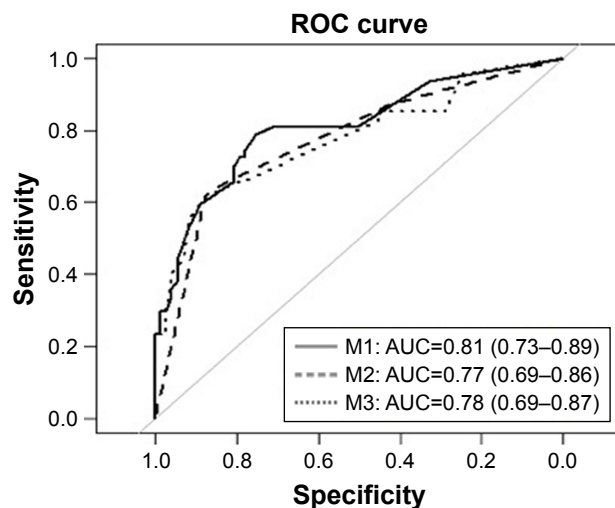

Figure 2 Multivariate analysis of adherence: ROC curves.
Notes: M1: Model that analyzed all parameters with P<0.10 in univariate analysis, with the exception of HbA1c. M2: Model that additionally excluded temporal horizon from the analysis. M3: Model that additionally excluded impatience from the analysis.
Abbreviation: ROC, receiver operating characteristic.

0.73–0.89), 0.77 (95% CI, 0.69–0.86) and 0.78 (95% CI, 0.69–0.87), respectively.

Determinants of HbA1c

In univariate analysis (the results of which are given in Table 4), the following characteristics were associated with HbA1c ≥8% (64 mmol/mol): long temporal horizon (OR, 0.85; 0.79–0.92; P<0.001), non-adherence to medication (OR, 45; 5.67–350.4; P<0.001), impatience in monetary choice (OR, 4.89; 1.7–14.06; P=0.003) and age ≥60 years old (OR, 0.28; 0.09–0.82; P=0.021). In multivariate analysis, two determinants were associated with HbA1c ≥8% (64 mmol/mol): non-adherence to medication (OR, 25.05; CI, 3.03–206.75; P=0.003) and long temporal horizon [OR, 0.90; CI, 0.84–0.98; P=0.011, AUC of the ROC curve =0.89 (CI 0.82–0.97)].

Determinants of temporal horizon

In univariate analysis (Table 5), long temporal horizon as determined by the event method was associated with long temporal horizon as determined by the story method (RR, 1.22; 95% CI, 1.17–1.27; P<0.001), non-adherence to medication (RR, 0.31; 95% CI, 0.23–0.43; P<0.001), a high HbA1c level (RR, 0.30; 95% CI 0.20–0.46; P<0.001), impatience (RR, 0.31; 95% CI, 0.23–0.43; P<0.001), existence of grandchildren (RR, 2.09; 95% CI 1.47–2.97; P<0.001), high score for depression (RR, 0.39; 95% CI 0.27–0.57; P<0.001), sadness (0.49; 0.33–0.73; P<0.001), pessimism (0.47; 0.31–0.70; P<0.001), social deprivation (RR, 0.47; 95% CI 0.33–0.67; P<0.001), older age (RR, 1.92; 1.35–2.74; P<0.001) and high degree of physical similarity at 1 year (1.02; 1.00–1.03; P=0.048), 5 years (1.01; 1.00–1.02; P=0.004) and 10 years (RR, 1.01; 95% CI, 1.00–1.02; P=0.001). In the multivariate analysis, three variables were associated with long temporal horizon: non-adherence to medication (RR, 0.49; 95% CI, 0.35–0.70; P<0.001), impatience (RR, 0.051; 95% CI 0.36–0.72; P<0.001) and existence of grandchildren (RR, 1.61; 95% CI 1.20–2.17; P=0.002).

Determinants of impatience

Similarly, in univariate analysis (Table 6), impatience was to be found associated with long temporal horizon (event method) (P<0.001), non-adherence to medication (P<0.001), high HbA1c level (P=0.024), high score for depression (P<0.001), sadness (P<0.001), pessimism (P=0.018), social deprivation (P<0.001), high physical

Table 4 Univariate analysis of HbA1c

Characteristics	Category	OR (95% CI)	*P*-value
Age (years)	≥60	0.28 (0.09–0.82)	**0.021**
Adherence (Girerd questionnaire)	Non-adherent	45 (5.67–350.4)	**<0.001**
Temporal horizon (events methods)		0.85 (0.79–0.92)	**<0.001**
Answer in the monetary choice	Impatient	4.89 (1.7–14.06)	**0.003**
Gender	Female	0.93 (0.35–2.48)	0.88
Activity	Stable	2.65 (0.57–12.3)	0.21
Marital status	Couple	1.85 (0.69–5.00)	0.22
Children	Yes	1.2 (0.24–6.06)	0.82
Grandchildren	Yes	0.47 (0.17–1.29)	0.14
BMI	>24	1.76 (0.60–5.18)	0.31
Smoking status	Quit	1.00	
	Never	1.09 (0.35–3.39)	0.89
	Active	1.67 (0.42–6.54)	0.46
Diabetes duration (years)		0.99 (0.93–1.04)	0.60
Retinopathy	Yes	1.68 (0.61–4.62)	0.31
Neuropathy	Yes	0.94 (0.35–2.54)	0.91
Stent	Yes	0.79 (0.2–3.08)	0.73
Treatment	Basal insulin	0.84 (0.31–2.25)	0.72
Similarity at 1 year		0.96 (0.91–1.02)	0.15
At 5 years		0.98 (0.96–1.01)	0.21
At 10 years		0.99 (0.97–1.01)	0.28
Social deprivation (EPICES questionnaire)	Score >30	2.04 (0.72–5.79)	0.18
Depression (Beck Depression Inventory)	Score >4	2.36 (0.73–7.63)	0.15
Sad (Beck Depression Inventory)	Yes	1.36 (0.45–4.09)	0.59
Pessimistic (Beck Depression Inventory)	Yes	1.66 (0.51–5.41)	0.40

Note: Bold figures represent statistically significant.
Abbreviation: BMI, body mass index.

Table 5 Univariate analysis of temporal horizon (events method)

Characteristics	Category	OR (95% CI)	*P*-value
Age (years)	≥60	1.92 (1.35–2.74)	**<0.001**
Grandchildren	Yes	2.09 (1.47–2.97)	**<0.001**
HbA1c	≥8% (64 mmol/mol)	0.30 (0.20–0.46)	**<0.001**
Adherence (Girerd questionnaire)	Non-adherent	0.31 (0.23–0.43)	**<0.001**
Temporal horizon (stories method)		1.22 (1.17–1.27)	**<0.001**
Similarity at 1 year		1.02 (1.00–1.03)	**0.048**
At 5 years		1.01 (1.00–1.02)	**0.004**
At 10 years		1.01 (1.00–1.02)	**0.001**
Social deprivation (EPICES questionnaire)	Yes	0.47 (0.33–0.67)	**<0.001**
Monetary choice	Impatient	0.31 (0.23–0.43)	**<0.001**
Depression (Beck Depression Inventory)	Yes	0.39 (0.27–0.57)	**<0.001**
Sadness	Yes	0.49 (0.33–0.73)	**<0.001**
Pessimistic	Yes	0.47 (0.31–0.70)	**<0.001**
Marital status	Couple	1.35 (0.92–1.98)	0.13
Children	Yes	1.34 (0.70–2.58)	0.37
BMI	>24	1.03 (0.67–1.61)	0.88
Smoking status	Quit	1	
	Never	0.73 (0.47–1.13)	0.15
	Active	0.7 (0.43–1.14)	0.15
Diabetes duration (years)		1.02 (1.00–1.04)	0.056
Retinopathy	Yes	1.16 (0.8–1.67)	0.44
Neuropathy	Yes	1.65 (1.15–2.38)	**0.007**
Stent	Yes	1.43 (0.85–2.41)	0.18
Treatment	Basal insulin	1.16 (0.8–1.67)	0.43

Note: Bold figures represent statistically significant.
Abbreviation: BMI, body mass index.

Table 6 Univariate analysis of impatience

Characteristics	Category	OR (95% CI)	P-value
Age (years)	≥60	0.62 (0.36–1.05)	0.07
Gender	Female	2.15 (1.23–3.75)	**0.007**
Grandchildren	Yes	0.89 (0.53–1.51)	0.68
HbA1c	≥8% (64 mmol/L)	1.23 (1.03–1.47)	**0.024**
Adherence (Girerd questionnaire)	Non-adherent	2.17 (1.59–2.96)	**<0.001**
Temporal horizon (event method)		0.82 (0.74–0.90)	**<0.001**
Similarity at 1 year		0.98 (0.95–1.01)	0.28
At 5 years		0.97 (0.94–0.99)	**0.006**
At 10 years		0.97 (0.96–0.99)	**<0.001**
Social deprivation (EPICES questionnaire)	Yes	11.49 (4.31–30.65)	**<0.001**
Depression (Beck Depression Inventory)	Yes	6.01 (2.27–15.87)	**<0.001**
Sadness	Yes	8.1 (2.63–24.88)	**<0.001**
Pessimistic	Yes	3.08 (1.21–7.84)	**0.018**
Marital status	Couple	0.27 (0.11–0.67)	**0.004**
Children	Yes	0.71 (0.27–1.90)	0.50
BMI	>24	0.66 (0.25–1.73)	0.40
Smoking status	Quit	1	
	Never	1.65 (0.66–4.13)	0.29
	Active	0.73 (0.28–1.93)	0.53
Diabetes duration (years)		0.96 (0.92–1.00)	0.066
Retinopathy	Yes	0.74 (0.35–1.56)	0.43
Neuropathy	Yes	0.74 (0.35–1.57)	0.43
Stent	Yes	1.32 (0.43–4.08)	0.63
Treatment	Basal insulin	0.98 (0.46–2.06)	0.95

Note: Bold figures represent statistically significant.
Abbreviation: BMI, body mass index.

similarity at 5 (*P*=0.006) and 10 years (*P*<0.001) and gender, with women giving the impatient answer more often in the fictive monetary scenario (OR=2.15; 95% CI, 1.23–3.75; *P*=0.007). In multivariate analysis, four variables were associated with impatience: social deprivation (OR, 12.92; 95% CI 3.61–46.29; *P*<0.001), non-adherence to medication (OR=2.17; 95% CI, 1.41–3.34; *P*<0.001), female gender (OR, 6.78; 95% CI 1.97–23.29; *P*=0.002) and long temporal horizon (event method) which was negatively associated with impatience (RR, 0.86; 95% CI 0.73–1.00; *P*=0.05).

MCA

MCA was used to detect and systematically explore, without an *a priori* hypothesis, the relationships among the different variables identified as relevant in the previous analysis. Three typologies were identified (Figure 3 and Table 7). The first group of patients (n=26) were characterized by adherence, HbA1c <8% (64 mmol/mol), older age, existence of grandchildren, long-duration diabetes, temporal horizon >5 years and patience in the monetary choice. These patients were not socially deprived, depressed, sad or pessimistic, according to their responses to Beck's questionnaire. They had quit smoking.

There were two typologies of non-adherent patients. The first group (n=59) were, like the group of adherent patients, not socially deprived, not depressed, sad or pessimistic; however, they were younger, had shorter diabetes duration and had no grandchildren. They had an intermediate temporal horizon (2–5 years); their HbA1c was ≥8% (64 mmol/mol); these patients either never smoked or were active smokers. The second group of non-adherent patients (n=35) exhibited the shortest temporal horizon (≤1 year), impatience and low physical similarity at 10 years. They were socially deprived, depressed and gave sad and pessimistic answers in the Beck's questionnaire.

Discussion
Main conclusion

This study was performed in hospitalized people with diabetes. Only one-third of the participants were adherent to medication. This rate of adherence was half of that reported in another study, also using the Girerd questionnaire, which was performed with the ENTRED cohort (n=3,767), representative of French residents with type 2 diabetes, having a mean HbA1c level of 7.0% (56 mmol/mol). In this population, 88% of the patients gave fewer than three positive answers to the
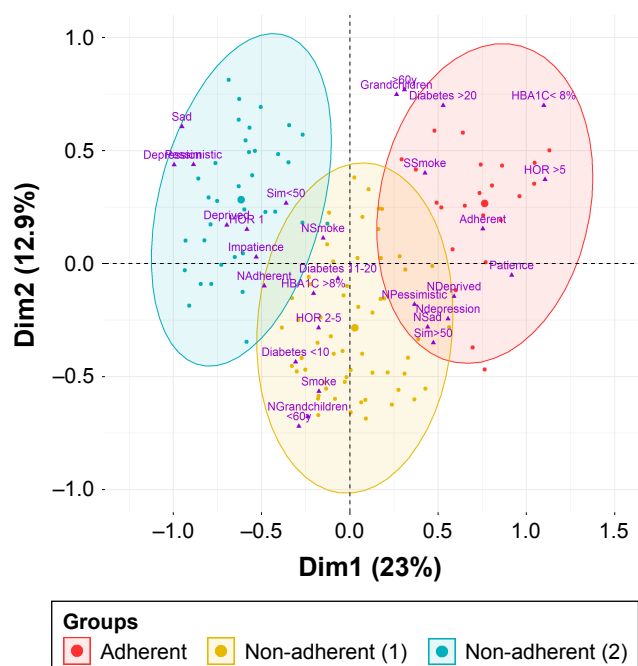
Figure 3 Multiplecorrespondence analysis.
Notes: Sim <50: 10-year similarity ≤50%. HOR 1: temporal horizon ≤1 year. NAdherent: non-adherent. NSmoke: never smoked. Diabetes 11–20: diabetes duration 11–20 years. Hor 2–5: temporal horizon 2–5 years. Diabetes <10: diabetes duration ≤10 years. Smoke: still smoking. NGrandchildren: no grandchildren. <60y: age <60 years old. Sim >50: 10-year similarity >50%. Ndepression: no depression. NSad: no sad answer in the Beck questionnaire. Npessimistic: no pessimistic answer in the Beck questionnaire. NDeprived: not socially deprived. SSmoke: quit smoking. HOR >5: temporal horizon >5 years. Diabetes >20: diabetes duration >20 years. >60y: age ≥60 years old. Each small dot represents a patient. Large dots represent the centers of typologies.

Girerd questionnaire.[19] The lower rate of adherence (39.2%) we report here is consistent with poorer metabolic control in these patients (mean HbA1c 9.8%), as adherence and HbA1c were demonstrated to be associated in the ENTRED study,[19] and it is also consistent with the known association between non-adherence and hospitalization.[2]

We observed, uniquely, an association between adherence to medication and patients' time projection. This was shown for two constructs describing time projection, patience and temporal horizon, which were the only two factors remaining to be associated with adherence to medication in multivariate analysis. This study also provided evidence of a link of adherence to medication and ability to imagine oneself physically in the future, to social deprivation and to depression.

Confirmation of known data and the novelty of this study

The association between impatience in monetary choice and adherence to medication is not new. We had demonstrated this link earlier in a cohort of 90 people with type 2 diabetes,[15] and this finding was later confirmed in a multicentric study.[20] These two studies also showed an association between impatience in monetary choice and poor metabolic control, as evaluated by HbA1c level, and the data presented in this report confirm this association. An association between impatience in monetary choice and medication adherence has also been demonstrated in asthma.[21]

By contrast, the link between temporal horizon and adherence to medication and HbA1c is novel because this construct has only been tested previously in the context of smoking.[13] The two constructs, patience/impatience and temporal horizon, may represent two aspects of time projection, namely, short- and long-term projection, respectively. The concept of expected physical similarity to current self, the third aspect of time projection, was investigated by Frederick,[16] who found that decreases in this value over time were sharper in younger people, especially in teenagers. However, Frederick observed no association between estimations of the degree of connection of now-me and future-me to the

Table 7 The three typologies of patients revealed by the multiple correspondence analysis

Adherent (n=26)	Non-adherent (1) (n=59)	Non-adherent (2) (n=35)
Age ≥60 years old	Age <60 years old	
Diabetes duration >20 years	Diabetes duration 11–20 years	
Temporal horizon >5 years	Temporal horizon 2–5 years	Temporal horizon ≤1 year
Similarity >50% in 10 years		Similarity in 10 years ≤50%
Patient		Impatient
Grandchildren	No grandchildren	
HbA1c <8% (64 mmol/mol)	HbA1c ≥8% (64 mmol/mol)	
Not socially deprived		Socially deprived
Not depressed		Depressed
Not sad		Sad
Not pessimistic		Pessimistic
Quit smoking	Never smoked or still smoke	

discount rate for the future in an intertemporal choice experiment.[16] Therefore, the link between the degree of similarity over time at 10 years and adherence, shown in the MCA undertaken in this study, is also novel. This link makes sense because adherence to long-term therapies may presuppose being able to imagine the future-me that I want to protect.[22]

Interestingly, the link between adherence and depression, present in the univariate analysis, was not confirmed in the multivariate analysis. However, when temporal horizon and impatience were excluded from multivariate analysis, depression was found to be an independent determinant of non-adherence. This is consistent with the link found between depression and perturbations in time projection.[23] Similarly, although social deprivation was shown to be associated with non-adherence to medication in univariate analysis, it was not present for any of the three models of multivariate analysis. Altogether, these data suggest that the effects of depression[24] and social deprivation[10] on patient adherence to long-term medication therapy is largely mediated by disturbance in time projection, which is consistent with deprivation being an independent factor associated with impatience, observed herein.

We observed in multivariate analysis that women gave an impatient answer more frequently than men in the monetary scenario (P=0.002). In literature, conflicting results have been found for the relationship between gender and time discounting:[25] during their reproductive period, women seem to exhibit patient behavior, but only in the follicular phase.[26] Thus, this finding may not be relevant for the women involved in this study, who tended to be older.

MCA provided further demonstration of the importance of time projection in orienting patients towards adherent or non-adherent behavior, as shown by the difference between the group of adherent patients and the first group of non-adherent patients, who were not experiencing social deprivation or depression. The main differences between these two groups of patients were the length of temporal horizon and existence of grandchildren, and the age and diabetes duration, which were lesser in non-adherent patients. One is tempted to speculate that the non-adherent patients in this group might become adherent later. They differed from a second group of non-adherent patients, who were characterized by the shortest temporal horizon of all, low expected physical similarity at 10 years and the presence of social deprivation, depression, sadness and pessimism. This cluster may indicate a more severe form of disruption in time projection (Table 7).

We must stress again that this study was performed in hospitalized patients who, therefore, were implicitly selected for a low rate of adherence and poor metabolic control. This had the advantage of ensuring the subjects were a more homogeneous group, making it possible to find unique links between time projection and patient adherence. However, different results may be observed in other settings. Thus, we recently published a study[27] performed on type 2 diabetes patients, who participated in a health survey panel on a regular basis and had, in general, well-controlled diabetes (mean HbA1c 7.15% [55 mmol/mol], median=6.65%) and low rates of non-adherence. In this setting, we observed, in an MCA, that adherent but socially deprived patients had little projection in the distant future (event method), suggesting that there is an effect of social deprivation on the personal temporal horizon, which would be consistent with the data we have reported herein. We also found that patience in monetary choice was associated with adherence, which is also consistent with the data presented here. However, in this study, non-adherent patients who, in general, were socially deprived, projected themselves well in the future, using the event method. To explain this unexpected observation, we speculated that there was effect of denial, which would be consistent with the fact that the story method, which evaluates the temporal horizon of someone else, did not show this effect.

In summary, although it has had initial negative reports,[28] we found that impatience in monetary choice is related to adherence to medication in diabetes[15,20,27] and asthma,[21] as well as to obesity,[29] being overweight[30,31] and to various addictions.[32] Short temporal horizon is linked to smoking habits,[13] which are then linked to adherence.[33] Finally, in another study performed in obese people with type 2 diabetes, we observed that self-declaration of prioritization of the future was linked to adherence to medication in an MCA.[34] Taken together, this accumulation of evidence renders plausible the concept that disruption in time projection is a factor in the determination of patient non-adherence to long-term therapies and can lead to the most severe forms of chronic diseases.

Limitations

This study was monocentric and cross-sectional, relying, as do many studies in this area, on self-report data without direct assessment. Furthermore, we excluded a priori those patients who were unable to read or understand the questionnaire. Additionally, explanations given to participants who had difficulty in understanding some questions, to avoid missing data, may have influenced the responses. The order of the questions may also have influenced the answers. However,

the data presented herein should nevertheless be robust enough to stimulate confirmatory studies.

Disruption in time projection: significance of the concept

Disruption in time projection as a player in both intentional and unintentional non-adherence

Adherence to long-term therapy has often been explained using socio-cognitive models, such as the Health Belief Model,[35] the Theory of Planned Behavior,[36] the Social Learning Theory,[37] and the Necessity-Concerns Framework.[38] Alongside these models, where non-adherence is largely "intentional", it has also been suggested that some forms of non-adherence may be "unintentional":[39] in the first case, patients, after weighing pros and cons, make a rational choice not to adhere while, for its part, unintentional non-adherence does not depend on the choice of the patient but on factors such as poor understanding of the prescription, difficulty of access to the prescribed medication, intervention of the patient's habits, lack of memory, defense mechanisms or simply irrationality.[12] In general, these unintentional aspects of non-adherence are not explored in cognitive questionnaires, such as the Beliefs about Medicine Questionnaire[40] or the Adherence Barriers Questionnaire.[41]

We propose that disruption in time projection, as described in this paper, plays a role in both intentional and unintentional non-adherence. Some people with disruption in time projection may prefer, either as a personal choice or under the pressure of external elements, such as social deprivation, to prioritize immediate rewards, ie, making a choice not to adhere. Others may not be conscious of the disruption in time projection they experience, which could, thus, be a novel source of cognitive bias[42,43] and, therefore, play a role in unintentional non-adherence. Incidentally, this dual effect on non-adherence represents a new argument for revisiting the distinction between intentional and unintentional non-adherence.[44]

Disruption in time projection as a loss of a protective mechanism: evolutionary insight into adherence

Time-projection ability may develop early in some children, as shown by Mischel's marshmallow test experiment, in which the ability to delay gratification at the age of 4 was shown to be linked to future positive outcomes, such as physical and psychological health, social competence and academic success.[45] The ability to delay gratification may have a neuronal basis, ie, the progressive development of the prefrontal cortex, the seat of the executive functions, which marks the transition from the adolescent to the adult brain,[46] or it may even have a genetic basis.[47,48] Evolutionarily, the development of foresight could represent a culmination of the hominization of *Homo sapiens sapiens*, who is endowed with reflexivity.[49] We suggest that this time-projection ability, which was a protective mechanism in pre-historical times, is now an element in being a "healthy adherer", and it explains the lower mortality rates in people adherent to a placebo.[50] In this general conceptual framework, disruption in time projection, whether innate or acquired, could result in a loss of this protective mechanism, leading to non-adherence to long-term therapies in chronic diseases.

Conclusion

Implications for medical practice

The link found between disruption in time projection and non-adherence to long-term medication therapies shown in this study may have important practical implications for teaching and practice of medicine. First, it may be important to present to "impatient patients" short-term rewards for adherence instead of the avoidance of long-term complications of their diseases. Next, giving full significance to the term *chronic* disease, this construct completes the bio-psychosocial model of medicine,[51] showing the importance of accounting specifically for various aspects of time projection, in addition to the potential deleterious effect of depression and social deprivation.

The general concept of person-centred medicine[52] encompasses temporality. Indeed, the philosopher Derek Parfit proposed that psychological continuity over time is what defines a person.[22] Thus, future doctors should be taught to ask patients not only about their history but also how they consider their future to enable diagnosis of the condition we termed here "disruption in time projection", with its three components: patience, temporal horizon and expected degree of physical similarity to one's self in the future.

Author contributions

GR designed the study and its analysis and wrote the paper. YB administered the questionnaire to patients and MB performed the statistical analysis. GR, YB, MB and VL contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work. No specific funding was provided for this study.

Disclosure

The authors report no conflicts of interest in this work.

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Appendix

Demographic data

- You are   male □   female □
- Your age: .... years
- Describe your employment situation: currently,
    ○ your employment is stable □ your employment is unstable □
    ○ you have no employment □ you are retired □ you are in search of employment □
    ○ you are a student   yes □   no □
    ○ you are disabled   yes □   no □
- You are single □ married □ living as a couple □ divorced □ widow □
- You have children   yes □   no □
- You have grandchildren   yes □   no □
- Your height: .... cm Your weight: .... kg
- Smoking habits: you never smoked □ quit smoking □ smoke □
- You have had diabetes since .... years (for instance 5 years)
- Last HbA1c level in patient record (completed by the resident after the interview) .... %
- Diabetes complications (completed by the resident): retinopathy yes □ no □
    ○ painful neuropathy   yes □   no □
    ○ stent   yes □   no □

Time projection

Patience/impatience

- If we offered to give you ∈ 500 today or ∈ 1,500 in a year from now, what would you choose? ∈ 500 today □ ∈ 1,500 in a year □

Temporal horizon

- Give a list of at least five events that could happen in your life (example: I will get married) with the age you think you will be when they happen:
    ○ Age:
    ○ Age:
    ○ Age:
    ○ Age:
    ○ Age:
- Here is the beginning of a story: Joe, drinking his coffee, starts to think of the future. He thinks that ...... Complete this story in three to four lines.
What is the duration of what you have imagined?
.... minutes .... days .... weeks .... months .... years

Similarity to current self

- Do you think that you will physically resemble your current appearance in 1 month, 1 year, 5 years and 10 years?

If your physical appearance completely changes, you would be unable to recognize yourself; this would mean 0% similarity to your current appearance. If there would be no change at all, this would mean 100% similarity to your current appearance.

Please rate the percentage of similarity to your current appearance (ranging from 0%=no similarity at all to 100%=complete similarity) for each of the following time frames: Degree of similarity (%)
In 1 month .... %
In 1 year .... %
In 5 years .... %
In 10 years .... %

Figure A1 Questions asked to the patients to collect their demographic data and to address time projection.
Note: Translated from French by the main author.