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Assessment of Intertemporal Preferences in Type-2 Diabetes Patients and Smokers

Evaluación de las preferencias intertemporales en pacientes con diabetes Tipo 2 y fumadores

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Abstract
The experiment assesses the role of cortisol concentration on bloodstream as correlate of the intertemporal choice and temporal discrimination in Type-2 Diabetes Mellitus (T2DM) patients and smokers. The participants were evaluated in a two independent computerized tasks allowed to obtain the temporal discount function and it's hyperbolic decay parameter (k), which refers to the tendency to discount the subjective value of future goods as a function of the delay to receiving them; and a temporal discrimination index (bisection point), this function relate the response proportion of "Long" stimuli with probe duration. The bisection point is the value at which responses to Short and Long stimuli occur with equal frequency. We analysed both parameters, then a comparisons of the temporal discount parameter $[F(2,147) = 79.858,\ p <,01]$ and time discrimination parameter $[F(2,147) = 49,51,\ p <,01]$ revealed statistically significant differences between control group and T2DM and smokers groups. We concluded that the choice for delayed rewards and the temporal discrimination of T2DM patients and smokers were influenced by the cortisol concentration in the bloodstream; the higher the concentration of cortisol in the bloodstream, the higher the likelihood to choose immediate rewards over larger delayed rewards and the higher the tendency to overestimate the passage of time. We propose to investigate the effects of salivary cortisol elevation levels through noninvasive pharmacologically induction on healthy adult humans, to extend the research line that assess the direct influence over intertemporal choice and temporal discrimination to increase the effect generality.

Resumen
El experimento evalúa el papel que tiene la concentración de cortisol en el torrente sanguíneo como correlato de elección intertemporal y discriminación temporal en pacientes con Diabetes Mellitus Tipo 2 (T2DM) y fumadores. Los participantes fueron evaluados en dos tareas computarizadas independientes que permitían obtener la función de descuento temporal y su parámetro de decaimiento hiperbólico (k), la cual hace referencia a la tendencia a descontar el valor subjetivo de bienes futuros como función de su demora de entrega; y un índice de discriminación temporal (punto de bisección), esta función relaciona la proporción de respuestas al estímulo "Largo" con la duración prueba. El punto de bisección es el valor en el cual las respuestas a los estímulos Corto y Largo ocurren con la misma frecuencia. Se analizaron ambos parámetros, por lo que las comparaciones en el parámetro de descuento temporal $[F(2,147) = 79.858,\ p <,01]$ y el parámetro de discriminación temporal $[F(2,147) = 49,51,\ p <,01]$ mostraron diferencias estadísticamente significativas entre el grupo control y los grupos T2DM y fumadores. Se concluyó que las elecciones por las opciones demoradas y la discriminación temporal de los pacientes con T2DM y fumadores fueron influenciadas por la concentración de cortisol en el torrente sanguíneo; a mayor concentración de cortisol en el torrente sanguíneo, hay una mayor probabilidad de elegir recompensas inmediatas sobre demoradas y una mayor tendencia a sobreestimar el paso del tiempo. Se propone investigar los efectos de la elevación de los niveles de cortisol salival a través de inducción farmacológica no invasiva en seres humanos adultos sanos, para extender la línea de investigación que evalúe la influencia directa sobre la elección intertemporal y la discriminación temporal para incrementar la generalidad del efecto.

Keywords
Cortisol; Impulsivity; Intertemporal choice; Humans; Time discrimination; Type-2 Diabetes Mellitus.
Palabras Clave
Cortisol; Diabetes Mellitus Tipo-2; Discriminación temporal; Elección intertemporal; Humanos; Impulsividad.

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1. Introduction

Unhealthy behaviours, such as tobacco smoking, excessive alcohol intake, physical inactivity and substance misuse, account for significant morbidity and mortality worldwide (Smith, Corrigan, & Exeter, 2012). Unhealthy behaviour frequently has a delayed effect on health, which leads to hypothesize that an individual's tendency to make unhealthy choices is related to their temporal discount rate, (Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian, 2012). A function which describes the pattern of discounting can be estimated by observing choices between delayed outcomes. Economic theories of rational behaviour assumes that goods tends to be discounted exponentially with delay (Samuelson, 1937). Here the discount rate, represents the constant proportional decrease in value with each added time period of delay. However, both humans and animals violate the exponential assumption of a constant proportional discount factor, appearing rather to discount rewards occurring in the immediate future more steeply than those in the distant future. The discount function estimated from observed choices is better accounted for by a hyperbolic function, written in its simplest form as follows:

$$V = \frac{A}{1 + (kD)} \tag{1}$$

Where V is the reinforce value, A is the reinforcer amount, D is the reinforcer delay, and k is a free parameter estimating how fast the value of the delayed option decays with increasing delay. Then, steep delay discounting is also known as impulsive decision making (Mazur, 1987; Rachlin & Green, 1972). Delay discounting is a robust empirical phenomenon with strong cross-species generality (Odum, 2011). In human's delay discounting has been related to maladaptive behaviours in clinical and pre-clinical settings (Madden & Bickel, 2010). In recent years a large number of studies have addressed this hypothesis, forming part of a growing endeavour to identify decision-making phenotypes which correlate with maladaptive behaviour (Montague, Dolan, Friston, & Dayan, 2012). Another aspect of human behaviour that may be related to impulsivity and delay discounting is the process of time discrimination (Berlin, Rolls, & Kischka, 2004; Rubia, Halari, Christakou, & Taylor, 2009). When people making choices between smaller immediate versus larger delayed outcomes, impulsive individuals tend to choose the smaller immediate outcome over the larger delayed reward more often (i.e., showing steeper discounting functions) than self-controlled participants. Delay discounting may be affected by how people perceives time; for impulsive individuals, the duration of the delay to the larger outcome may be perceived longer than that perceived by less impulsive individuals, thereby increasing the likelihood to choose the smaller immediate outcome (Rubia et al., 2009; Wittmann & Paulus, 2008).

1.1 Stress Systems and Cognitive Processes

Regarding to stress systems, two primary systems particularly involved in setting on the stress response are the hypothalamus—pituitary—adrenocortical axis (HPA) and the sympatho-adrenomedullary (SAM) systems. When the HPA axis responds to stress, corticotropin is released from the hypothalamus (CRH) and it is secreted by the paraventricular nucleus (PVN) of the hypothalamus which in turn leads to the release of ACTH from the pituitary and stimulates the secretion of glucocorticoids (GCs) from the adrenal cortex. Once the GCS is elevated, it exerts a negative feedback via the pituitary, hypothalamus, and hippocampus (Heuser & Lammers, 2003). By acting on a wide array of target tissues, GCs are important for successful adaptation . These include mobilizing energy into the bloodstream from storage sites in the body, increasing cardiovascular tone and delaying long-term processes in the body that are not essential during a crisis, such as feeding, digestion, growth, and reproduction. Some of the actions of GCs help mediate the stress response, while other, slower actions counteract the primary response to stress and help re-establish homoeostasis. Over the short run, epinephrine mobilizes energy and delivers it to muscles for the body's response. The GC cortisol, however, promotes energy replenishment and efficient cardiovascular function.

GCs also affect food intake during the sleep-wake cycle. Cortisol levels, which vary naturally over a 24-hour period, peak in the body in the early-morning hours just before waking. This hormone helps produce a wake-up signal, turning on appetite and physical activity. This effect of glucocorticoids may help explain disorders such as jet lag, which results when the light-dark cycle is altered by travel over long distances, causing the body's biological clock to reset itself more slowly. Until that clock is reset, cortisol secretion and hunger, as well as sleepiness and wakefulness, occur at inappropriate times of day in the new location.

Acute stress also enhances the memory of earlier threatening situations and events, increases the activity of the immune system, and helps protect the body from pathogens. Cortisol and epinephrine facilitate the movement of immune cells from the bloodstream and storage organs, such as the spleen, into tissue where they are needed to defend against infection. GCs do more than help the body respond to stress. They also help the body respond to environmental change. In these two roles, glucocorticoids are in fact essential for survival.

Thus, GCs and glucose regulation are closely linked in regulating stress. When cortisol levels increase, also blood glucose levels increase (Khani & Tayek, 2001). Several studies have focused on the effect of T2DM on HPA axis functioning (Lee et al., 1999) looking for increasing HPA axis activity, these results, however, have been inconsistent across studies perhaps due to differences in protocols and different characteristics of the subjects that participated in those studies. Reports of elevations in basal cortisol levels in plasma are inconsistent, with one study showing elevated levels (Lee et al., 1999) and another reporting no alterations (Andrews, Herlihy, Livingstone, Andrew, & Walker, 2002). A study using salivary cortisol measures observed elevated evening levels in T2DM (Liu, Bravata, Cabaccan, Raff, & Ryzen, 2005).

Cortisol levels among individuals with diabetes were shown to be associated with glycemic control (Oltmanns et al., 2006). Further suggesting that HPA axis dysregulation is linked to T2DM.

It is well established that both T2DM and elevated levels of GCs affect some cognitive processes (Ryan & Geckle, 2000; Starkman, Gebarski, Berent, & Schteingart, 1992). For example, T2DM is associated with deficiencies in memory, attention, and executive functions (Biessels, ter Braak, Erkelens, & Hijman, 2001; Ishizawa, Kumano, Sato, & Iwamoto, 2010). The hippocampus, which is essential for declarative memory, is reported to be of small size among elderly individuals with T2DM (den Heijer et al., 2003). Also, hippocampal volume reductions have been reported among non-diabetic individuals with insulin resistance (Convit, Wolf, Tarshish, & de Leon, 2003). Research suggests that chronic elevations of GC levels can have deleterious effects on the hippocampus (McEwen, 2000). It is important to note that this structure of the brain, which is affected by both elevated GC levels and T2DM, plays a central role in HPA axis feedback inhibition; in addition, the hippocampus has the highest co-localization of insulin and GC receptors in the brain (Jacobson & Sapolsky, 1991), adding to the possible links between impaired HPA axis regulation and T2DM, then cortisol levels among individuals with diabetes have been associated with glycemic control, suggesting that HPA axis dysregulation is linked to T2DM (Oltmanns et al., 2006).

1.2 Temporal Discount and Time Discrimination

Perhaps one of the most documented finding in the intertemporal choice literature is that individuals discount the value of delayed rewards, the hyperbolic model (Mazur, 1987), capture the observation that individuals make farsighted plans when outcomes are distant, but reverse their choices in favour of short-term rewards when the future is reached (see Kalenscher & Pennartz, 2008). There is now a substantial body of empirical evidence demonstrating time-inconsistent discounting in both human (Kirby & Herrnstein, 1995) and animals (Ainslie, 1974; Rachlin & Green, 1972); among normal people and substance abusers (Bickel, Odum, & Madden, 1999; Kirby & Petry, 2004); and for various types of outcomes, including time, money, health, job offers, and life savings (Cairns & Van der Pol, 1997; Hesketh, Watson-Brown, & Whitely, 1998; Zauberman & Lynch, 2005).

Because temporal discounting in humans is influenced by several factors such as hormones, like cortisol (Takahashi, 2004), cigarette-smoking status of individuals (Ohmura, Takahashi, & Kitamura, 2005), genre (Lucas & Koff, 2010), and age (Read & Read, 2004) and impulsive behaviour is a stable-personality trait (Odum, 2011). Individuals differ dramatically in their psychophysiological responses to stress, and their brain functions and behavioural performances also vary with their stress responsiveness (Lupien, Maheu, Tu, Fiocco, & Schramek, 2007; Pruessner et al., 1997; Sapolsky, 2015). For example, Starcke, Polzer, Wolf, and Brand (2011) found large interindividual differences in endocrine stress reactions and an association between individual's cortisol response to stress and decision-making behaviour, although no significant behavioural changes in decision-making were found under stress compared with the non-stress control condition. For the specific case, smoking increases ACTH and cortisol levels. This response appears to require quite intense intake, involving more than one cigarette (Gilbert, Meliska, Williams, & Jensen, 1992; Kirschbaum, Wüst, & Strasburger, 1992), and has been attributed to nicotine exposure (Newhouse et al., 1990; Seyler Jr, Fertig, Pomerleau, Hunt, & Parker, 1984). Interestingly, it has recently been established that nitric oxide is an inhibitory mediator of nicotine-induced HPA activity, providing a direct link between inflammatory processes and the HPA activation stimulated by smoking (Gadek-Michalska & Bugajski, 2004).

The relationship between smoking, cortisol and nicotine is important for at least three reasons. First, the HPA axis is implicated in addictive processes, as discussed earlier. Second, heightened levels of cortisol have a range of adverse effects on biological processes relevant to long-term health, including lipid profiles, immune function, central adiposity, bone mineral density and reproductive function (Steptoe & Ayers, 2004). Cortisol may therefore mediate some of the effects of smoking on health outcomes such as cardiovascular disease and the metabolic syndrome. Third, cortisol is highly sensitive to psychological stress. Smoking cessation is stressful for many smokers, and this may lead them to fail in quit attempts. It has been proposed that cortisol is directly involved in this process, and that changes in cortisol following smoking cessation may predict early relapse (al'Absi, Hatsukami, Davis, & Wittmers, 2004; Frederick et al., 1998).

Knowing the role of cortisol in determining impulsive behaviour will help to develop medical methods and clinical trials to prevent neuropsychiatric disruptions associated with impulsivity and drug addictions, then it's important to examine how individuals having different levels of stress hormones (i.e., cortisol) differ to one another in choice situations. For these reasons, the goal of the present study is to examine the role of cortisol in determining intertemporal choice. To accomplish this goal, the intertemporal preferences (temporal discount task) and the time discrimination (temporal bisection task) of T2DM patients and cigarette smokers were assessed systematically in the present study. It was hypothesized that high levels of cortisol, like those present in T2DM and cigarette-smoking individuals, cause impulsive behaviour and an overestimation of time delaying presentation of larger reward (Yi & Landes, 2012).

2. Method

2.1 Participants

Human participants ($n = 150$) were recruited through advertisements run in a local hospital. The mean age of the individuals was 47.3 years (range $= 21 - 69$), and they were assigned to one of three groups (50 individuals in each group)

as follows: (1) the never-smoking-cigarette group consisted 24 males and 26 females; (2) the ever-smoking-cigarette group, consists of 25 males and 25 females on average, participants smoked 20.2 cigarettes/day (range: 15–40 cigarettes/day) and scores on the Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) were 5.9 (range: 3–10); (3) and the T2DM-group with 24 males and 26 females. Since T2DM and smoking status are associated with neuroendocrinological substrates (cortisol) mediating the relations between time perception and temporal discount rates, were examined between the three groups.

2.2 Experimental Protocols

Blood samples of all participants were collected between 8 : 00 and 8 : 30AM for the assessment of cortisol and glucose, after completing the experimental tasks. Participants were given instructions not to eat or drink anything except for water previously to the blood sample assessment, and to refrain from physical exercise before the experiment.

2.3 Apparatus/instruments

The experiment was conducted in a single session, with each participant working on the same computer. Participants could attend the session one of the days and times scheduled for the data collection. All stimuli were presented and responses were recorded on computers running a program written by the first author in Visual Basic.Net 2005 software.

2.4 Procedure

After reading and signing the informed consent, participants completed two behavioural tasks, a delay discounting task and a temporal bisection procedure. In the delay-discounting task, the participants made choices between two hypothetical amounts of money, one delivered immediately and the other amount of money delivered later in time (see description below for details). A block randomization design was used to determine the order of administration of the behavioural tasks.

2.4.1 Delay Discounting

Before the experiment began, the participants made 6 training choices to familiarize themselves with the main procedure. During this session, the participants choose between an immediate reward and a delayed reward, at a random interval value. (i.e, 1 year or 1 month). The first choice at each delay was between the delayed amount and an immediate amount that was equal to half of the delayed amount (e.g., $\$10,000$ in 1 month or $\$5,000$ now). For each of the subsequent choices at that delay, the amount of the immediate reward was adjusted based on the participant's previous choice. If the participant chose the immediate reward, then its amount was decreased on the following trial; if the participant chose the larger, delayed reward, then the amount of the immediate reward on the next trial was increased. The size of the adjustment to the immediate reward after the first choice was half of the initial amount of that reward. Subsequently, the size of the adjustment to the immediate reward decreased with each successive choice and was always equal to half of the previous adjustment, rounded to the nearest Mexican pesos. This iterative procedure converged rapidly on the immediate amount subjectively equivalent to the delayed amount (Myerson, Green, Hanson, Holt, & Estle, 2003). The subjective value of each delayed amount was determined at each of seven delays (1 week, 1 month, 6 months, 1 year, 3 years, 5 years, and 10 years).

2.4.2 Data Analysis

These data points were pooled across individuals of the same group to compute the mean indifference point for each of the seven delays and the discounting function was obtained with the group's means using Mazur (1987) hyperbolic-decay model. The obtained values of k were used to conduct a one-way analysis of variance (ANOVA).

2.4.3 Temporal Bisection Procedure

In this task, the participants were asked to judge whether the presentation of a stimulus (i.e., a small circle, 200 pixels of diameter) displayed on the computer's screen center was of a short (S) 1.0 s or a long (L) duration, 4.0 s. Training was splitted into 2 phases. During the Pre-Training Phase participants learned the reference durations and received feedback. During the Probe Duration Phase intermediate durations were added (1.0, 1.5, 2.0, 2.5, 3.0, 3.5 and 4.0s) and feedback was withheld. Participants were instructed to indicate which reference duration they perceive the stimulus duration was closest too (Allan & Gibbon, 1991; Wearden, 1991). The participants' perception of time was estimated by computing the proportion of choice responses for the long duration sample (long / long + short) across presentations of sample durations. The proportion of long choice responses was plotted as a function of the sample's duration, and a two parameter logistic function was fitted:

$$\frac{1}{1+\left(\frac{t}{T50}\right)^{\varepsilon}} \tag{2}$$

where T_{50} and ε are free parameters expressing the bisection point and the slope of the function, respectively. The bisection point was analysed using one-way analysis of variance (ANOVA).

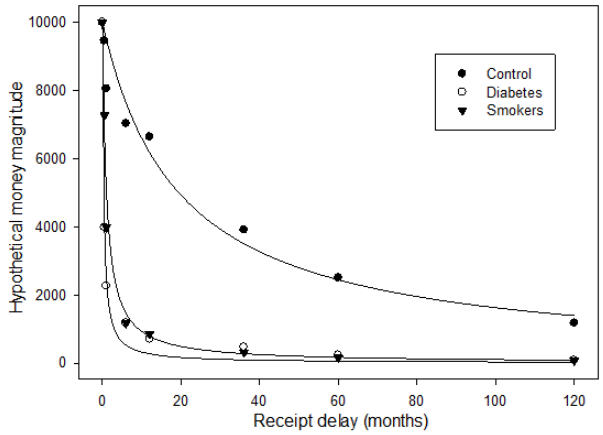
3. Results

To organize this section, the data from the delay discounting task (assessing impulsivity) will be describe first, and then the relation between impulsive choice and time perception. The section concludes with the analysis of the correlations among measures. We adopted a conservative significance level, $p < .01$, instead of the common use of the $p < .05$ index of significance level.

3.1 Delay Discounting

The magnitude of the hypothetical amount of money was plotted in Figure 1 against the receipt delay in months, best

Figure 1. Temporal discounting functions. The subjective value (i.e., hypothetical money magnitude) is plotted as a function of delay until receiving a reward. The graph shows the data from T2DM ($k = 3.67$), smokers ($k = 1.62$) and control ($k = 0.13$) groups. The curved lines are the best fitting discounting functions (Equation (1)).



fitting lines connecting data points were generated with equation (1). Filled circles stand for the control group, unfilled circles for the T2DM group, and triangles for the cigarette-smoking group. For the latter groups, the rate of discounting (k) was 3.67 and 1.62 respectively. Figure 1 shows steeper discounting functions than that it shows for the control group ($k = 0.13$). Preference for the immediate alternatives was greater in the T2DM group (i.e., stepper discount function) than that observed in the smoking group; both groups however show the same pattern of impulsivity (i.e., similar choices) across delays compared with control group.

The control group clearly shows a strong preference for the delayed alternatives (i.e., less impulsive choices that the other two groups). Estimates of k equation (1) obtained from the discounting functions of the individuals were assessed for differences in impulsivity between groups. A one way analysis of variance (ANOVA) showed significant differences between groups $F(2,147) = 79.858, p < 0.01$. In Table 1, it can be appreciated the Post-hoc Sheffé's test, using it, we can test each pair of means in ANOVA to see whether a specific difference exists, at $p < .01$.

Figure 1 Temporal discounting functions. The subjective value (i.e., hypothetical money magnitude) is plotted as a function of delay until receiving a reward. The graph shows the data from T2DM ($k = 3.67$), smokers ($k = 1.62$) and control ($k = 0.13$) groups. The curved lines are the best fitting discounting functions in Figure 1.

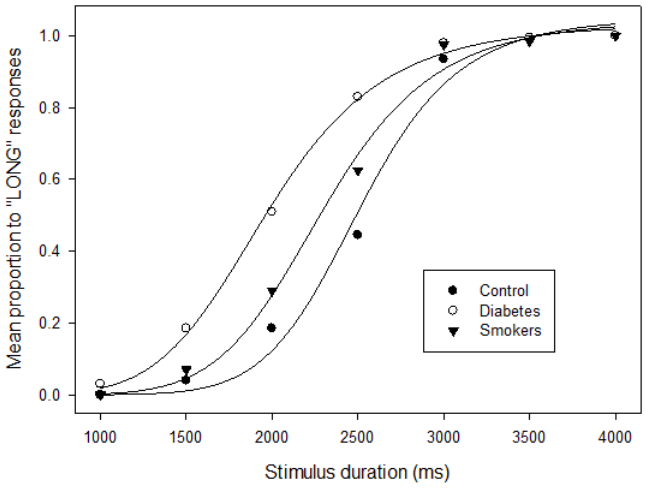
We assess the genre variable and found no significant statistical differences between the impulsivity indexes for control group $[F(1,48) = 2,26, p > 0,05]$, T2DM group $[F(1,48) = 3,04, p > 0,05]$ and smokers group $[F(1,48) = 3,18, p > 0,05]$.

Table 1. Post-hoc Sheffé's test for the impulsivity index in the three groups.

	Control	Diabetes	Smokers
Control		**	**
Diabetes	**		x
Smokers	**	x	

Note. $(** : p < .01; * : p < .05; x : p > 0,05)$.

Figure 2. Proportion of "LONG" responses plotted against stimulus duration. The graph shows the data from T2DM ($T_{50} = 1860$), smokers ($T_{50} = 2134$) and control ($T_{50} = 2511$) groups. The curved lines are the best fitting logistic functions (Equation (2)).



3.2 Time Discrimination

Figure 2 shows the mean proportion of "LONG" responses plotted against stimulus duration for each group. A detailed inspection of the psychophysical functions suggests that in all groups the proportion of long responses increased with the stimulus duration, the bisection points were indicated in Figure 2. The psychophysical functions from T2DM and smokers groups compared to the control group, appear to be systematically shifted to the left, the bisection point of the T2DM and smoking groups is smaller than that observed in the control group, with the former group making choices before the expected time or arithmetic mean, causing the bisection point to be an overestimated time of the discrimination index. The T2DM group, however, shows a greater overestimation than both the cigarette-smoking and the control group. One way ANOVA showed significant differences in the bisection point in all the groups $[F(2,147) = 49,51, p < 0,01]$. In Table 2, it can be appreciated the Post-hoc Sheffé's test, showing the statistical differences between groups.

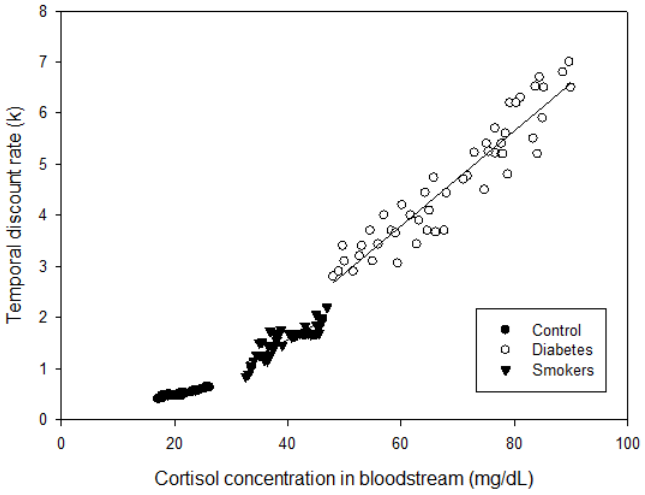
For the different groups, Figure 3 shows the correlations between the impulsivity index (k) and the concentration of

Table 2. Post-hoc Sheffé's test for the bisection point in the three groups.

	Control	Diabetes	Smokers
Control		**	*
Diabetes	**		x
Smokers	*	x	

Note. $(** : p < .01; * : p < .05; x : p > 0,05)$.

Figure 3. Scatterplot of impulsivity index (k) as a function of the cortisol concentration in the bloodstream for the T2DM, control and smoker's groups.



cortisol in the bloodstream (mg/dL). Figure 4 the correlations between the bisection point (ms) and the concentration of cortisol in the bloodstream (mg/dL).

The Table 3, shows the mean value, standard deviation and correlations between cortisol concentration and glucose concentration, both in bloodstream of each group, the significance level was set at $p < 0,01$, we found all the groups meet the statistical criteria. The Table 4 shows a multiple comparison correlation of each group between the impulsivity index in delay discounting task as a function of cortisol concentration in bloodstream and the bisection point in temporal bisection procedure as a function of cortisol concentration in bloodstream. We can observe only the control group didn't

Table 3. Descriptive statistics and correlation indexes of the groups between cortisol and glucose concentration in bloodstream.

Group	Cortisol (mg/dL)	Glucose (mg/dL)	r (p<0,01)
Control	21.4±7.8	75.8±7.7	0,9678
Diabetes	66.4±14.0	178.0±26.4	0,9527
Smokers	38.0±9.9	86.2±8.2	0,9932

Figure 4. Scatterplot of bisection point (ms) as a function of the cortisol concentration in bloodstream for the three groups.

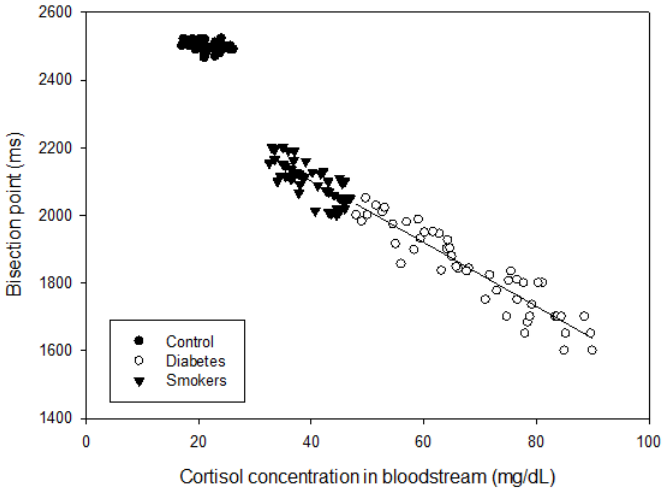


Table 4. Correlation indexes of the groups between impulsivity index (k), bisection point (ms) and cortisol concentration (mg/dL) in bloodstream.

Group	Impulsivity index (k)	Bisection point (ms)
Control	0.9433	0.4247
Diabetes	0.9423**	0.9299**
Smokers	0.8779**	0.7723*

Note. Positive correlations between cortisol concentration in bloodstream and impulsivity index and bisection point in diabetes and smokers groups. $(** : p < .01; * : p < .05)$.

meet the statistical criteria $(p < 0,01)$.

We found higher correlation between glucose concentration and cortisol concentration in the bloodstream in every group; in fact correlations were similar among groups as we can see in Table 1, suggesting the main effect of the cortisol as a modulator of glucose concentration in bloodstream in all groups. Correlations in Figure 4 were negative because the increases in cortisol levels in the bloodstream were related with an overestimation of time intervals, then the participants seemed to perceive the "short" stimuli as longer than they really are, so the participants classified as "long" stimuli. This case is clearly seen in T2DM and smoking groups. The control group showed no significant difference in the time estimate $(r = -0.2423; p > 0.05)$. We assess the genre variable and found no significant statistical differences between the bisection point for control group $[F(1,48) = 1,14, p > 0,05]$, T2DM group $[F(1,48) = 2,21, p > 0,05]$ and smokers group $[F(1,48) = 2,67, p > 0,05]$.

4. Discussion

The goal of this study was to examine the role of cortisol in controlling impulsivity and intertemporal choice. To our

knowledge, this is the first study assessing the relation between concentrations of cortisol in the bloodstream and impulsive choice using delay discounting and temporal bisection procedures. The degree of delay discounting in the T2DM and smokers groups as a dependent measure of the cortisol levels on the bloodstream shows an impulsive pattern of choices, as we can see in Figure1 and Figure3. We propose that high levels of decay in the subjective value of the assessed monetary options in participants with T2DM and smokers is due to a dysregulation of cortisol levels in the bloodstream, eliminating the explanation that people with T2DM had higher indexes of impulsivity as a result of higher glucose levels in the bloodstream (Ishizawa et al., 2010).

We discard the effect of genre over the impulsivity index and bisection point in the three groups , the sample could be restricted to male participants to minimize confounds from hormonal fluctuations during the female cycle (Woods, Mitchell, & DiJulio, 2010). The regulation of glucose levels is given primarily by the release of insulin and cortisol in the bloodstream; these physiological variables appear to have a stronger predictive function than glucose. In fact, as can be seen in Figure1 and Figure 3, the trend in the response patterns between T2DM and smoking groups is practically the same, so we can argue that in both groups the result of their higher rates of devaluation of the monetary options isn't due to higher glucose levels in the bloodstream (as seen in the group of smokers) but simply because the cortisol release leading to being stressed regardless if they belong to the T2DM group or smoking; providing a new and plausible correlation for the phenomenon studied. Meanwhile it has found the same effect on temporal estimation task, which was dependent on the levels of cortisol in the bloodstream in the same groups, gives greater robustness to the effect of this hormone in the patterns of choice and estimation in the corresponding experimental tasks.

Notably, the control group, showing a particular behavioural performance contrast, the cortisol levels were related with a moderate decay pattern of subjective value of the options evaluated in temporal discounting task, as found in other investigations where the control groups exhibit the same pattern of responding. Meanwhile, in the time estimation task, control group showed temporal indices close to the arithmetic ($2500ms$) where again the levels of cortisol in the bloodstream technically had no effect on participants because on average the control group showed a point of bisection of $2511ms$.

We must highlight that our measure of time discrimination was not influenced by the reaction time to make a choice, and thus may provide a good estimate of the relation between delay discounting and temporal discrimination. A negative correlation between steep delay discounting (high values of k) and overestimation of the time discrimination (low values of bisection point) was found, our data suggested that people that chose more impulsively also had a tendency to overestimate how time elapses for T2DM group ($r = -0.8381; p < 0,05$) and for smokers group ($r = -0.6759; p < 0,05$). Thus, one reason that a person may not value the delayed rewards very much is that the delay seems longer than it really does, this finding shows that people who are more impulsive on the delay discounting task tend to pay less attention to the temporal bisection procedure, therefore tend to emit an overestimated responses of the presented duration value. It can be concluded that the effect of the cortisol levels in bloodstream is related with impulsive choice behaviour and temporal discrimination. In a careful meta-analysis of well over one hundred studies, Block, Hancock, and Zakay (2010) established that human adults' discrimination of the passage of time differs according to whether they are forewarned that they will need to make a timing judgement, and are therefore actively attending to its passage (prospective time estimation), or whether they are required to make an unexpected, after-the-fact judgement of the passage of time (retrospective time estimation). And finally, this difference is heavily modulated by cognitive load, showing a classic cross-over interaction in which either prospective or retrospective judgements are longer depending on whether the participant experiences high or low cognitive load.

The positive strong correlation (see Table 2) between the glycemic and stress indexes founded in the present study, confirmed that cortisol and the concentration of glucose in the bloodstream is related with choice and temporal discrimination in humans with T2DM and those addicted to nicotine. Evidence from both animal and human studies supports that high concentrations of cortisol in the bloodstream have deteriorating effect on cognitive processes (McEwen, 2000). Only a few studies, however have suggested that this might be also the case of people diagnosed with T2DM. The present study found in individuals with T2DM and smokers that high concentrations of cortisol are correlated to the impairment in cognitive abilities in their impulsive choices in delay discounting and temporal bisection procedures.

The present study aim was to examine how impulsive choice and time overestimation are related with high levels of cortisol in the bloodstream. We found clearly in the T2DM and smokers groups an overestimation of the time, in other words, the passage of time was more quickly and then it will be a good predictor of how the participants will discount the value of a delayed monetary reward. Future studies should focus on the degree to which this effect is replicable in different populations using different techniques to manipulate temporal discrimination. For example, a person who overestimates the passage of time could receive training on veridical time to show that improving the accuracy of temporal discrimination helps to retain the value of a delayed reward, with important implications for the understanding and treatment of impulsivity. Another research line will be the psychopharmacological manipulation of cortisol levels in adult healthy humans to target time-dependent effects, these possibly results suggest that the physiological effects of acute cortisol induction, may increase temporal discounting and time overestimation.

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