

Excessive Physical Activity and Decision Making: Focus on Anorexia Nervosa

Stefano Erzegovesi¹, Riccardo Maria Martoni^{1*}, Martina Oliva¹, Laura Bellodi^{1,2}, Regina Gregori Grgic^{1,2} and Anna Ogliari^{1,2,3}

¹Department of Clinical Neurosciences, I.R.C.C.S. San Raffaele-Turro, Via Stamira D'Ancona, 20, 20127, Milan, Italy

²Developmental Psychopathology Unit, Vita-Salute San Raffaele University, Via Olgettina, 58, 20132, Milan, Italy,

³Faculty of Psychology, Vita-Salute San Raffaele University, Via Olgettina, 58, 20132, Milan, Italy

These authors contributed equally to the work

*Corresponding author: Riccardo Maria Martoni, Department of Clinical Neurosciences, I.R.C.C.S. San Raffaele-Turro, Via Stamira D'Ancona, 20, 20127, Milan, Italy, Tel: +39226433315, E-mail: martoni.riccardo@hsr.it

Citation: Stefano Erzegovesi, Riccardo Maria Martoni, Martina Oliva, Laura Bellodi, Regina Gregori Grgic, et al. (2022) Excessive Physical Activity and Decision Making: focus on Anorexia Nervosa. J Neurosci Neuropsych 5: 102

Abstract

Excessive physical activity (EPA) is a complex symptom in Anorexia Nervosa (AN), but little is known about its underlying mechanisms. A recent hypothesis suggested a link between EPA and impaired decision-making abilities in AN-EPA. The present study objective is to assess how the reward system functions under PA. The sample collected data on healthy Athletes (HC-A), Non-Athletes (HC-NA) and AN. AN group contains people with and without EPA. We recruited 30 female patients with AN and, as control groups, 30 females HC-A and 30 females HC-NA. Decision-making was assessed through both monetary reward and PA reward. PA reward was assessed through a newly modified version of IGT, in which monetary rewards were substituted with PA rewards. The results showed that the four groups performances did not differ when the reward was monetary. However, when the reward consisted in physical activity, HC-A performed better than HC-NA. Moreover, AN patients with EPA performed significantly worse than HC groups. Our finding did not reach statistical significance to discriminate performances between AN subgroup. Our findings did not permit to discriminate performances between AN subgroups, because of their smaller size than HC-A and HC-NA groups. These preliminary results should be considered as an important first step, that could pave the way to further research on the connection between EPA and AN and to support new treatments of this symptom.

Keywords: Anorexia Nervosa; Excessive Physical Activity; Iowa Gambling Task; Reward; Athletes

Introduction

Anorexia Nervosa (AN) is an eating disorder characterized by weight loss, difficulties in maintaining an appropriate body weight and distorted body image [1]. Excessive physical activity (EPA) has been recognized as one of the most prevalent AN symptoms: 31% to 80% patients with AN showed EPA [2]. Furthermore, EPA has been associated with several health problems, such as bone fractures, osteoporosis, cardiovascular symptoms [3,4], and diagnosis-specific issues, such as lower fat percentage, greater severity of the psychopathology, longer inpatient treatment, quicker relapse and worse treatment outcome [5-8].

Psychosocial models describing the role of physical activity on mental health show that moderate PA lowers levels of anxiety and depression [9-10] and that it provides an opportunity for social interaction, improves self-efficacy and perceived competence, and facilitates interaction with the natural environment [11]. Though, when PA is excessive, psychological symptoms as depression and anxiety seem to occur [10-12]. Moreover, excessive training, particularly with a high degree of aerobic fitness [10], can be associated with symptoms such as sleep disturbance, loss of weight and appetite, reduced libido, irritability, emotional dysregulation [10-13]. In the last decades, EPA has been investigated under neurobiological and neuropsychological perspectives as well.

The most accredited neurobiological model of EPA is the Activity-Based Anorexia (ABA) [14-15]. In this model, rodents experience food restriction while having free access to the running wheel. The majority of them, after the restriction, become hyperactive, spending more time in the running wheel in comparison to the days before [15,16]. Because of the enhanced movement, rodents lose weight and, in addition, they start to restrict food intake spontaneously, even when they have free access to their meal [17]. Nowadays, researchers have explained EPA behavior in different ways. A recent review highlighted how the investigation of decision-making during the ABA model could help to better understand the relationship between impaired decision-making abilities and EPA in AN [18].

From a neuropsychological perspective, decision-making abilities have been extensively analyzed on patients with AN, mainly using standard rewards (e.g. money) [19-26] or stimuli concerning food or calories [27,30]. The most accepted explanation for these findings is that an altered reward related decision-making under uncertainty would represent a trans-diagnostic neurobiological process that underlines psychopathological behaviors [29]. More in details, patients with AN tend to restrict the food intakes, strive for thinness, and make EPA with little reflection, consideration and understanding the long-term consequences of this unhealthy and risky behavior.

Literature seems to suggest a link between reward system functioning and EPA in AN [18], but there is only one study that investigated this hypothesis [30]. In this study, the authors assessed for the first time the attentional processing in response to pictures depicting activity (i.e., a girl practicing sport) and inactivity (i.e., a girl at rest) using eye-tracking. Sample was based on AN patients and two healthy control groups, one of athletes and one of non-athletes. Their aim was to examine if the reward system functioning towards PA stimuli was different among the three groups. Previous studies [31-33] had investigated gaze behavior when subjects were exposed to other motivationally salient stimuli as food, alcohol or faces, showing that gaze is preferentially allocated to rewarding stimuli. The results of the study of Giel and colleagues revealed that AN patients and athletes had a stronger bias in attentional engagement towards active stimuli in comparison to non-athletes. As a future line of research, the authors point out that the role of PA in the reward system functioning of AN patients might be better investigated inducing a stronger self-reference during the task [30].

The aim of our study is to further deepen the knowledge about the relationship between decision-making under uncertainty and EPA in AN. Indeed, it is widely known that reward plays a key role in exercise behavior for active individuals [34], but it still is unclear why in patients with AN this element could turn into EPA. Our hypothesis is that deficient decision-making under uncertainty influences the exercise reward mechanism: patients may not be able to stop doing physical exercises due to an inappropriate reward evaluation and the difficulty to evaluate long-term consequences of EPA. We realized that to date there is no adequate task in literature, which allows a sufficiently immersive experience that considers a PA reward as truthful as possible to test our hypothesis. Therefore, we conceived a task in which participants had a first-person perspective in a video of a runner on an athletic track. We

thought that the first-person view and the sound of both footsteps and breath could provide participants with a more intense and immersive experience than a static image. We decided to use a modified version of IGT task, that we called Physical Activity Iowa Gambling Task (PA-IGT), where rewarding mechanisms are more directly called into play, utilizing a mechanism of PA wins and PA losses depending on the subjects' choice (see methods for more info).

We investigated if PA-IGT was able to detect differences between our four samples: Athletes, Non-Athletes, Anorexia Nervosa patients with Excessive Physical Activity (AN-EPA) and Anorexia Nervosa patients without Excessive Physical Activity (ANWEPA). Based on IGT results, we expected Athletes and Non-Athletes not to differ in their performances and the patients' groups to obtain worse performances, without significant differences between AN-EPA and AN-WEPA. Concerning PA-IGT, we expected Athletes to perform better than Non-Athletes and better than AN patients (i.e. AN-EPA and AN-WEPA). Between the patients' groups (i.e. AN-EPA and AN-WEPA), we expect AN-EPA to obtain the worse score. A similar study maintained the tripartition of the experimental sample in healthy athletes, healthy non-athletes and AN patients [30], while we further divided our sample into AN with and without EPA. As a result, we expected AN-EPA to show a worse performance than AN-WEPA, being the EPA symptom specific of this sample.

Materials and Methods

Participants

Thirty female patients with AN and sixty female healthy control (HC) participants took part in the study (Table 1). The HC group was recruited from general population and it was split into two subgroups: thirty subjects were classified as 'athletes' (HC-A) and the other thirty as 'non athletes' (HC-NA). Athletes were considered as participants who made a reiterated and continuous experience of sport for more than five consecutive years during their lives.

The three groups (i.e. patients with AN, HC athletes and HC non-athletes) were age-, education- and gender- matched. Within the AN group, participants were also divided into two subgroups: 17 subjects who did 5 or more hours of PA every week (AN-EPA) and 13 subjects who did less than 5 hours of PA every week (ANWEPA). Under a clinical point of view, EPA in AN can assume a variety of forms and clinicians followed psychopathological guidelines which are well described in literature [35-36].

The inclusion criteria were: a) age between 14 and 45 years; b) absence of mental disability and c) the capacity to sign the informed and the privacy consent. The clinical sample was recruited from I.R.C.C.S. San Raffaele Turro. All patients with AN met DSM-5 diagnostic criteria for AN as the primary clinical diagnosis. Patients were recruited from the hospital ward and from the hospital outpatient clinic. The study was an addition to the routine care of the patients and there was no compensation for the time of the participants.

The exclusion criteria for the HC group, were: a) present or lifetime psychiatric disorder; b) overweight (> BMI 25); c) brain injury with loss of consciousness; d) positive anamnesis for neurological syndromes and cognitive disorders; e) psychotropic treatment and f) familiarity with psychiatric disorders. Furthermore, neither psychology student, nor psychologist participated to the study, since many of them already knew the rules of one of the tasks we used (IGT, Iowa Gambling Task) [37]. The experiment was conducted in accordance with the Declaration of Helsinki and the Ospedale San Raffaele Ethical Committee.

	HC		AN	
	Athletes	Non Athletes	AN-EPA	AN-WEPA
Age	22,47 # 5,89	22,47 # 6,06	20,53 # 3,19	25,54 # 6,79
Weight ^*°v	56,10 # 6,22	55,60 # 6,22	40,30 # 4,60	42,92 # 5,32
BMI ^*°v	20,50 # 1,80	20,59 # 2,15	15,30 # 1,76	15,18 # 1,84
BDI II ^*°v	7,87 # 7,57	10,37 # 7,90	23,00 # 15,58	22,62 # 10,33
EDI-2 ^*°v	36,27 # 26,70	33,80 # 24,89	90,71 # 52,22	86,77 # 33,20
STAI 1 ^*°v	40,13 # 11,83	40,57 # 11,17	56,59 # 13,99	54,15 # 12,41
STAI 2 ^*°v	32,17 # 9,09	34,57 # 11,43	51,29 # 13,85	51,77 # 13,61
PI *v	36,57 # 26,60	38,10 # 27,92	53,76 # 32,70	65,38 # 36,34
IGT	5,27 # 24,36	-1,57 # 23,56	-0,29 # 35,39	-0,31 # 18,53
PAIGT §^*°	16,60 # 25,11	-10 # 25,18	-35,53 # 27,94	-21,23 # 38,56

BMI: Body Mass Index; BDI-II: Beck Depression Inventory II; EDI-2: Eating Disorder Inventory-2; STAI 1-2: State-Trait Anxiety Inventory-Y; PI: Padua Inventory; IGT: Iowa Gambling Task; PA-IGT: Physical Activity Iowa Gambling Task. [§: HC-A≠HC-NA; ^HC- A≠AN-EPA; *HC-A≠ANWEPA; HC-NA≠AN-EPA; ^HC-NA≠ANWEPA; #AN- EPA≠ANWEPA]

Table 1: Descriptive Statistics of the four subgroups. Data presented as mean ± SD. Mann-Whitney Test (p<.05)

Measure Section

Self-Reports

The psychological assessment consisted in four self-report questionnaires. The Beck Depression Inventory-II (BDI-II) [38] evaluates depressive symptoms. It has four response options, ranging from 0 to 3, and provides 4 symptoms categories based on the score obtained: 0–13 (minimal depressive symptoms), 14–19 (mild depressive symptoms), 20–28 (moderate depressive symptoms) and 29–63 (severe depressive symptoms). The Italian version of the BDI-II was used in this study, which showed high internal consistency (i.e., Cronbach $\alpha = 0.80$) and good test-retest reliability after 1 month ($r = 0.76$).

The Padua Inventory (PI) [39] evaluates Obsessive-Compulsive Disorder symptoms and it comprises 60 items, scored on a 5-points scale, which ranges from 0 to 4. We used in this research the total score. Higher scores indicate more severe symptoms. The original Italian version shows very good internal consistency for the scale (i.e., Cronbach $\alpha = 0.94$). The test-retest correlation (30 days apart) was equal to 0.78 for males and to 0.83 for females [39].

The Eating Disorder Inventory-2 (EDI-2) [40] evaluates Eating Disorders symptoms. The EDI-2 comprises 91 questions. Each question is on a 6-point scale (ranging from “always” to “never”), rated 0-3. We used a total score in this paper. Cronbach’s alpha values range from 0.82 to 0.93 for each sub-scale.

The State-Trait Anxiety Inventory-Y (STAI-Y) [41] evaluates anxiety symptoms. IT includes 20 items for assessing state anxiety and 20 items for trait anxiety. All items are evaluated on a 4-point scale, with a total score that ranges from 20 to 80 for both state and trait anxiety subscales. The STAI-Y showed high internal consistency (i.e., Cronbach $\alpha = 0.93$ for state anxiety, and Cronbach $\alpha = 0.90$ for trait anxiety).

The Iowa Gambling Task (IGT)

The IGT is a task assessing decision-making abilities using a monetary reward [37]. During IGT, subjects are required to gain as much money as possible, choosing from four different decks of cards. The decks differ in two aspects: the long-term advantageousness and the losses frequency. In particular, deck A and B are disadvantageous decks, containing cards with high immediate rewards, but also even higher losses, leading up to a long-term disadvantage. In contrast, decks C and D are advantageous decks, because even if they give lower immediate rewards, in the long-term they result in gains for their even lower losses. In addition, while decks A and C have frequent smaller losses (i.e. 5 losses every 10 cards), decks B and D have infrequent higher losses (i.e. 1 loss every 10 cards). Participants have to select 100 cards choosing freely from the various decks and trying to establish a strategy that makes them gain money in the long-term. When subjects start the task, they receive an initial loan of 2000 €. Moreover, in case they lose this sum of money through disadvantageous choices, they receive other 2000 € to continue, doubling however their initial debt.

The Physical Activity Iowa Gambling Task (PA-IGT)

The PA-IGT is our modified version of IGT: we substituted the classical monetary reward with a PA reward (Fig. 1). Differently from IGT, during PA-IGT participants watch a video of a run on an athletic track, filmed from the perspective of the person who runs. The participant is asked to run as fast as she/he can, gaining and losing velocity points (which consisted in an acceleration or deceleration of the running, respectively) in the same way she/he would win or lose money in the original IGT, namely through 100 selections from the decks A, B, C and D. The structure of frequency of rewards-punishment was the same of standard IGT. The purpose is to utilize the rewards distributions of IGT, which are already validated and well documented, and transpose them to the new PA-IGT version, in order to create an emotionally salient task about PA.

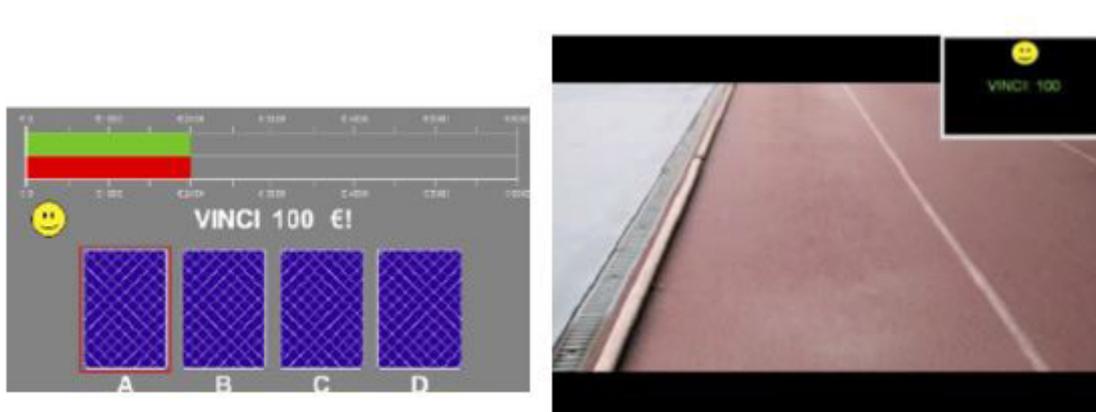


Figure 1: Screenshot of the Italian version of the IGT (a) and PA-IGT (b): the first win from deck A

The PA-IGT was programmed with MATLAB R2014b (The MathWorks, Inc.), which was enabled to automatically modify the velocity of the video (presented through the VideoLAN software VLC) after each subjects’ click on the A, B, C or D key. Because each subject had to perform both tasks, we modified the decks’ order: both the variable advantage-disadvantage and the variable frequent-infrequent loss were inverted, but the two good decks and the two bad decks remained close to each other, so that the

participant used a similar cognitive load to spatially associate the advantageous decks and the disadvantageous one. Moreover, while participants in IGT used the mouse or the touchpad to click on the four decks they saw on the screen, in PA-IGT they used four keys on the keyboard, which were renamed A, B, C and D. The video of PA-IGT has been shot in the 200 meters athletic track Campi dello Zerbino in Genoa. The audio of the runner's breath and steps has been edited on the video afterwards. Moreover, the video looped after one track lap and its velocity (V) was accelerated to a maximum of $4x$ and decelerated to a minimum of $0.3x$, depending on the amount of win and loss of each deck selection. V was directly proportional to the quantity of VP (Velocity Points) achieved by the participant. In fact, the video started with $V=2x$, which corresponded to the 2000 VP of the initial debt. Moreover, changes in V were recalculated at each moment, according to the equation $V = VP/1000$. Over 4000 VP, V remained $4x$, because an increase in V over $4x$ would have damaged the quality of the video and of the audio. It is important to underline that none of our experimental subjects managed to exceed 4000 VP and that it was an extremely rare condition to achieve. Moreover, between 0 and 300 VP, V remained $0.3x$, since the video could not decelerate below $0.3x$. As in IGT, when the amount of VP reached 0 or a negative number, 2000 additional points were reaccredited to continue the task with the formula: $NEW\ TOTAL\ VP = 2000 + TOTAL\ VP$, where $TOTAL\ VP$ could have been 0 or a negative number. In this case, velocity was calculated as $NEW\ TOTAL\ VP/1000$. During the task, the video was opened automatically by MATLAB and ran with VLC, which permitted to accelerate or decelerate the video with a precision of $0.1x$ (i.e., 100 VP), maintaining the fluidity of the video. For this reason, in some cases V was rounded (e.g., values <50 VP did not change the velocity of the video, while values ≥ 50 represented a change of the velocity by $\pm 0.1x$).

Since the only difference between IGT and PA-IGT is the video regarding PA, the results obtained could be due to the addition of any sort of video, not necessarily of a PA video. In fact, subjects could base their decisions on the speed-changes feedback (e.g. optical flow; breath) or on every other additional information compared to the monetary reward of IGT. In this case, the type of reward used in PA-IGT (i.e. PA) would be irrelevant for the results. Therefore, we performed a control experiment in order to assess whether the differences observed were not caused by the addition of any sort of video different from a PA video. For this reason, we substituted the PA video with a new one presenting sea waves, breaking on the beach. We called this new task Wave-IGT. The aim was to use a video, which maintained the relevant features of the PA video (i.e. changes in velocity of the visual (i.e. the movement of the waves) and of the auditory stimuli (i.e. the sound of the waves)), but which did not involve any kind of PA. 11 AN patients and 33 HC, divided in Athletes and Non-Athletes, participated in the control study. Comparing the samples through Mann-Whitney tests, we found that the three subgroups did not differ in the performances at the Wave-IGT. These results seem to strengthen our hypothesis that the differences found in PA-IGT actually concern the type of reward (i.e. PA) and not just the features of the video (i.e. changes in velocity of the visual and of the auditory stimuli).

Procedure

All participants underwent both a decision-making and a psychological assessment. Before starting the experimental session, sociodemographic (i.e. age, education and marital status), PA (i.e. hours spent doing PA and level of performed PA) and clinical data (i.e. weight, height, presence/absence of menstrual cycle, familiarity with Psychiatric Disorders and, only for patients with AN, onset, duration and drug therapy) were collected. The decision-making assessment consisted in the administration of two computerized tasks: the Iowa Gambling Task (IGT) and its newly modified version, the Physical Activity Iowa Gambling Task (PA-IGT). Then subjects answered the psychological assessment (see 2.2.)

During the experimental session, (ca. 45 min), subjects started with one of the two tasks (i.e. IGT or PA-IGT), continued completing the self-report questionnaires and ended with the remaining task (i.e. IGT or PA-IGT). The order in which the tasks were presented was balanced among subjects and groups. Any plausible learning bias due to the presentation order was excluded through dedicated analyses.

Statistical Analysis

Data were analysed using IBM SPSS Statistics 20. We verified the distribution of each variable through Kolmogorov-Smirnov Test. Since variables had a non-normal distribution, we proceeded with non-parametric comparisons. We used Kruskal Wallis Tests to

compare the four subsamples both in self reports and behavioral tasks (i.e. HC-A (N=30); HC-NA (N=30); AN-EPA (N=17); ANWEPA (N=13)). Where Kruskal Wallis Test showed a significance threshold under 0,05, we used Mann-Whitney Test for one to one comparisons between subsamples (i.e. HC-A vs HC-NA; HC-A vs AN-EPA; HC-A vs ANWEPA; HC-NA vs AN-EPA; HC-NA vs ANWEPA; AN-EPA vs ANWEPA).

Results

Self-report questionnaires

The whole comparison between groups was performed with Kruskal Wallis test. Groups showed significative differences in any self-report questionnaire: Back Depression Inventory II [BDI-II, H (3, N= 90) =25,53 p =,000], Eating Disorder symptoms [EDI-2, H (3, N= 90) =35,15 p =,000], Padua Inventory [PI, H (3, N= 90) =9,59 p =,022] and State-Trait Anxiety Inventory-Y [STAI 1: H (3, N= 90) =22,34 p =,000] [STAI 2: H (3, N= 90) =34,49 p =,000].

As expected, Mann-Whitney Tests showed that Athletes and Non-Athletes subgroups did not differ in any of the self-report questionnaires (all $p > ,150$). ANEPA and ANWEPA patient subgroups did not differ in any of the self-report questionnaires (all $p > ,483$). Both AN groups showed higher depressive symptoms, higher Eating Disorder symptoms, higher Obsessive-Compulsive Disorder symptoms and both higher state and trait anxiety symptoms than both HC groups.

IGT and PA-IGT total scores

Comparing IGT and PA-IGT for the four subgroups, the Kruskal Wallis Tests showed that the samples did not significantly differ from each other in the IGT total score [H (3, N= 90) =,639 p =,887], while they differed in PA-IGT [H (3, N= 90) =32,68 p =,000].

For this reason, we decided to continue the analysis only for the PA-IGT comparisons (Figure 2). Taking in exam the total scores of each subgroup, we found that Athletes differ from all other samples significantly in terms of better performances (HC-A vs HC-NA, Z: -3,639; $p = ,000$; HC-A vs AN-EPA, Z: -5,062; $p = ,000$; HC-A vs ANWEPA, Z: -3,174; $p = ,002$). Moreover, Non-Athletes perform PA-IGT significantly better in comparison to AN-EPA (Z: -2,948, $p = ,003$). No significant difference between Non-Athletes and the ANWEPA sample (Z: -,967, $p = ,339$) and AN-EPA and ANWEPA (Z: -1,340, $p = ,180$) emerged.

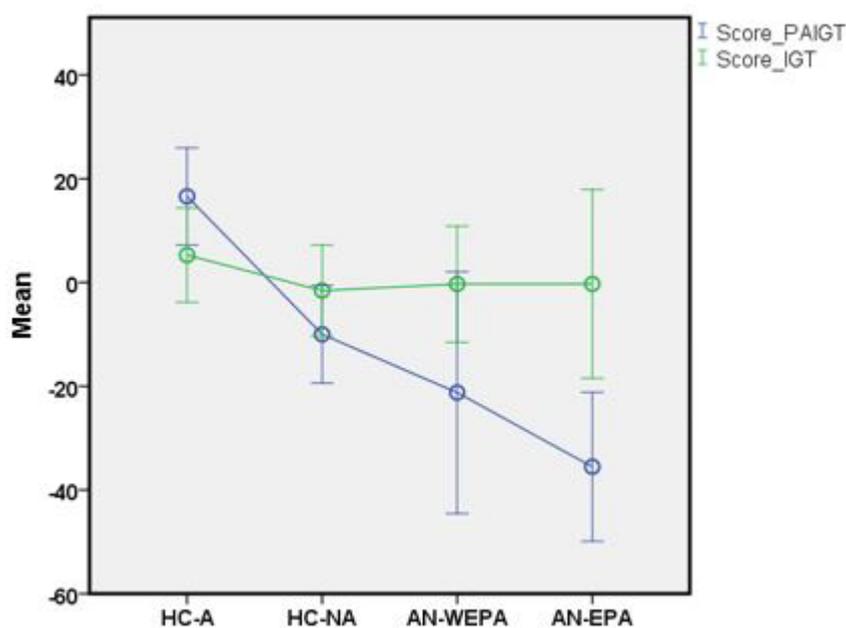


Figure 2: Subsamples comparison in IGT and PA-IGT total score. Error Bars (95% Confidence Interval) are showed

Discussion

The aim of our pilot study was to evaluate decision-making strategies with a new task (i.e. PA-IGT) that we conceived to study a mechanism of PA wins and PA losses depending on the subjects' choice. Our hypothesis was that the well documented AN impaired decision-making under uncertainty [29] could influence the exercise reward mechanism: we thought that AN patients may not be able to stop doing PA due to an inappropriate reward evaluation and the difficulty to evaluate long-term negative consequences. To verify this hypothesis, we compared four groups: HC-Athletes, HC-Non-Athletes, Anorexia Nervosa patients with Excessive Physical Activity (AN-EPA) and Anorexia Nervosa patients without Excessive Physical Activity (ANWEPA). This distinction has been led by an assumption: we conceived Athletes as people with high rewarding effect from physical activity and maintained decision-making abilities under uncertainty, while we thought that Non-Athletes could maintain decision-making abilities under uncertainty, but without any physical exercise relevance.

The main result of our pilot study was that PA-IGT was able to detect differences between HC-Athletes and HC non-athletes; in fact, we found significant difference between these two groups. In accordance with other studies [42-44], we expected Athletes to be able to deal with PA and its consequent reward in a functional way. This means for example having the ability to tolerate the frustration of postponing the rewarding feeling, to control the eventual bad consequences of self behavior and, if necessary, to fix it. Athletes were namely PA experts and we confirmed the hypothesis that reward plays a pivotal role in exercise behavior for active individuals [34]; in other words, an athlete without any difficulty in decision-making abilities under uncertainty should be able to regulate the rewarding effect of physical exercise in order to reach a better performance in the task. A possible interpretation of non-athletes performance could be that they could be unaccustomed to this type of reward and to its functional management or PA could simply be less rewarding for them. Interestingly, using IGT as a control condition, we found no difference between groups, suggesting that winning money could be a salient rewarding stimulus for both groups.

Then, we compared both HCs group with the AN groups. We performed nonparametric analysis and it's worth clarifying that our results should be considered as preliminary signals in a novel and complex field of research.

Under a clinical perspective, we found that both AN groups had higher scores at each survey in comparison to HC. This indicates that the AN sample showed, in line with other studies [19,23,24], more severe levels of anxiety (i.e. STAI), obsessive-compulsive traits (i.e. PI); eating disorders (i.e. EDI) and depressive symptoms (i.e. BDI). We also found that ANEPA showed worse performance in PA-IGT than HC-A and HC-NA and this result could be explained by the fact that a more emotionally salient reward amplifies the differences between the samples, since it targets the difficulty of the ANEPA patients more specifically. In line with this result, some studies show that AN patients (i.e. ANEPA) exaggerate PA and disregard its negative consequences on their health, as they only focus on immediate high rewarding sensations [2,46,47].

Our study did not find any difference between ANEPA and ANWEPA; future studies should clarify if this result should be considered as an effect of the small sample or if our method to classify AN patients should be more standardized before assessing any specific issue. In a recent study, sub-grouped AN patients in hyperactive girls and non-hyperactive ones, using an interesting mixed procedure from sporting activity prior to the disease onset level of hyperactivity evaluated during the hospitalization [45]. We did not use this procedure and we classified patients on the reported PA (i.e. 5 or more hours of PA every week). We took this information from the patient's psychiatrist and from exploratory questions to the patient about her PA habits. In future studies it could be more noteworthy to add objective PA measures (e.g. actigraph (Sense Wear Armband)) in order to obtain both a more precise classification of ANEPA and ANWEPA and a comparison between the real and the perceived patients' activity. To our knowledge, just one previous study focused on a similar aspect [30], investigating the process of hyperactivity-related information, comparing Athletes, Non-Athletes and AN patients. The authors found that AN patients and Athletes had a stronger bias in attentional engagement toward active stimuli. Though, the stimuli used by Giel and colleagues [30] were images of a woman engaged in an active or inactive situation and the same authors proposed as future studies to create PA stimuli, which induce a stronger self-reference during the task.

We also found in IGT no differences between any AN patients' group and the HC sample. Other studies showed no differences between any AN patients' group and the HC sample [15,17], but we also found other studies where AN patients show less decision-making abilities in comparison to HC [19, 23, 25].

Our study proposed an alternate version of IGT, able to assess the reward-ing effect of physical activity on decision-making under uncertainly. In our opinion this novel task could help to deepen the understanding of neurobio- logical mechanism that underpin EPA in AN. However, we know that the study has several limitations and for these reasons it should be considered as a pilot study.

Future studies, with larger samples, should consider the effect of the dura-tion of illness on cognitive functioning; in fact, it is well documented that poorer cognitive performances were present in patients with long-term evolution of the disorder [48].

PA-IGT used a motor linked behavior as rewarding stimulus, whereas Bechara and colleagues treated motor and cognitive impulsivity separately both in HC and psychiatric samples (i.e. see [49]). Future studies should clarify the relationship between IGT and PA-IGT with different levels of analysis (i.e. impulsivity questionnaires and/or imaging studies).

Results should be replicated in other samples of Athletes and non-athletes and future studies should assess EPA with standard measures (better with a dimensional method) in order to evaluate if PA-IGT is sensitive to this clinical feature.

Finally, the control video did not measure the effect of having first-person point of view. Future studies with PA-IGT structure should have a more detailed control. For example, using as stimulus a similar first-person video that is not athletic like riding a motorcycle and making it go faster.

Author Contributions: “Conceptualization, S.E., R.M.M., M.O., L.B., A.O.; methodology, R.M.M., M.O., R.G.G., A.O.; software, R.G.G.; formal analysis, S.E., R.M.M., R.G.G., A.O.; investigation, R.M.M., M.O.; resources, n/a.; data curation, M.O., R.G.G.; writing—original draft preparation, S.E., R.M.M., M.O., R.G.G., A.O.; writing—review and editing, S.E., R.M.M., M.O., R.G.G., A.O.; visualization, X.X.; supervision, S.E., L.B., A.O.; project administration, n/a; funding acquisition, n/a. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Ethics Committee of Ospedale San Raffaele. Protocol Code: AN_EPA 2016 on 12-15-2016.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: All authors are grateful to Mattia Giuliani, Giulia Columpsi and Alberto DJ Ceresa for the support in revising the last version of the paper and to Claudia Baruffaldi for the help collecting data.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Zipfel S, Giel KE, Bulik CM, Hay P, Schmidt U (2015) Anorexia nervosa: aetiology, assessment, and treatment. *Lancet Psychiatry* 2: 1099-1111.
2. Hebebrand J, Exner C, Hebebrand K, et al. (2003) Hyperactivity in patients with anorexia nervosa and in semi-starved rats: evidence for a pivotal role of hypoleptinemia. *Physiol Behav* 79: 25-37.
3. Bratland-Sanda S, Sundgot-Borgen J, Rosenvinge JH, Ro O, Hoffart A, et al. (2010) Physical fitness, bone mineral density and associations with physical activity in females with longstanding eating disorders and non-clinical controls. *J Sports Med Phys Fitness* 50: 303-10.
4. Haddad FS, Bann S, Hill RA, Jones DH (1997) Displaced stress fracture of the femoral neck in an active amenorrhoeic adolescent. *Br J Sports Med*, 31: 70-2.
5. Dalle Grave R, Calugi S, Marchesini G (2008) Compulsive exercise to control shape or weight in eating disorders: prevalence, associated features, and treatment outcome. *Compr Psychiatry* 49: 346-52.
6. Hechler T, Rieger E, Touyz S, Beumont P, Plasqui G, et al. (2008) Physical activity and body composition in outpatients recovering from anorexia nervosa and healthy controls. *Adapt Phys Activ, Q*, 25: 159-73.
7. Solenberger S (2001) E. Exercise and eating disorders: a 3-year inpatient hospital record analysis. *Eat Behav*, 2: 151-68.
8. Dittmer N, Jacobi C, Voderholzer U (2018) Compulsive exercise in eating disorders: proposal for a definition and a clinical assessment. *Journal of eating disorders*, 6: 42.
9. McMahon EM, Corcoran P, O'Regan G, et al. (2017) Physical activity in European adolescents and associations with anxiety, depression and well-being. *European child & adolescent psychiatry*, 26: 111-22.
10. Paluska SA, & Schwenk TL (2000) Physical activity and mental health: current concepts. *Sports medicine (Auckland, N.Z.)*, 29: 167-80.
11. Lubans D, Richards J, Hillman C, F et al. (2016) Physical Activity for Cognitive and Mental Health in Youth: A Systematic Review of Mechanisms. *Pediatrics*, 138: e20161642.
12. Peluso MA & Guerra de Andrade LH (2000) Physical activity and mental health: the association between exercise and mood. *Clinics (Sao Paulo, Brazil)*, 60: 61-70.
13. Budgett R (1990) Overtraining syndrome. *British journal of sports medicine* 24: 231-6.
14. Hall JF & Hanford PV (1954) Activity as a function of a restricted feeding schedule. *J Comp Physiol Psychol*, 47: 362-3.
15. Routtenberg A & Kuznesof AW (1967) Self-starvation of rats living in activity wheels on a restricted feeding schedule. *J Comp Physiol Psychol* 64: 414-21.
16. Aoki C, Sabaliauskas N, Chowdhury T, et al. (2012) Adolescent female rats exhibiting activity-based anorexia express elevated levels of GABA(A) receptor alpha4 and delta subunits at the plasma membrane of hippocampal CA1 spines. *Synapse*, 66: 391-407.

17. Chowdhury TG, Chen YW, Aoki C (2015) Using the Activity-based Anorexia Rodent Model to Study the Neurobiological Basis of Anorexia Nervosa. *J Vis Exp* (105): e52927.
18. Lamanna J, Sulpizio S., Ferro M, Martoni R, Abutalebi J, Malgaroli, A (2019) Behavioral assessment of activity-based-anorexia: how cognition can become the drive wheel, *Physiology & Behavior*, 202: 1-7
19. Adoue C, Jaussent I, Olie E, et al (2015) A further assessment of decision-making in anorexia nervosa. *Eur Psychiatry*, 30: 121-7.
20. Bosanac P, Kurlender S, Stojanovska L, et al. (2007) Neuropsychological study of underweight and “weight-recovered” anorexia nervosa compared with bulimia nervosa and normal controls. *Int J Eat Disord*, 40: 613-21.
21. Cavedini P, Bassi T, Ubbiali A, et al (2004) Neuropsychological investigation of decision-making in anorexia nervosa. *Psychiatry Res*, 127: 259-66.
22. Chan TW, Ahn WY, Bates JE, et al (2014) Differential impairments underlying decision making in anorexia nervosa and bulimia nervosa: a cognitive modeling analysis. *Int J Eat Disord*, 47: 157-67.
23. Liao PC, Uher R, Lawrence N, et al (2009) An examination of decision making in bulimia nervosa. *J Clin Exp Neuropsychol*, 31: 455-61.
24. Reville MC, O'Connor L, Frampton I (2016) Literature Review of Cognitive Neuroscience and Anorexia Nervosa. *Curr Psychiatry Rep*, 18: 18.
25. Tchanturia K, Liao PC, Forcano L, et al (2012) Poor decision making in male patients with anorexia nervosa. *Eur Eat Disord Rev*, 20: 169-73.
26. Tchanturia K, Liao PC, Uher R, Lawrence N, Treasure J, Campbell IC (2007) An investigation of decision making in anorexia nervosa using the Iowa Gambling Task and skin conductance measurements. *J Int Neuropsychol Soc*, 13: 635-41.
27. Cowdrey FA, Finlayson G, Park RJ (2013) Liking compared with wanting for high- and low-calorie foods in anorexia nervosa: aberrant food reward even after weight restoration. *Am J Clin Nutr*, 97: 463-70.
28. Godier LR, Scaife JC, Braeutigam S, Park RJ (2016) Enhanced Early Neuronal Processing of Food Pictures in Anorexia Nervosa: A Magnetoencephalography Study. *Psychiatry J*, 1795901.
29. Wu M, Brockmeyer T, Hartmann M, Skunde M, Herzog W, et al. (2016) Reward-related decision making in eating and weight disorders: A systematic review and meta-analysis of the evidence from neuropsychological studies. *Neurosci Biobehav Rev*. 61: 177-96.
30. Giel KE, Kullmann S, Preissl H, et al. (2013). Understanding the reward system functioning in anorexia nervosa: crucial role of physical activity. *Biol Psychol*, 94: 575-81.
31. Castellanos EH, Charboneau E, Dietrich MS, et al (2009). Obese adults have visual attention bias for food cue images: evidence for altered reward system function. *Int J Obes (Lond)*, 33: 1063-73.
32. Chakrabarti B, & Baron-Cohen S (2011) Variation in the human cannabinoid receptor CNR1 gene modulates gaze duration for happy faces. *Mol Autism* 2: 10.
33. Giel KE, Friederich HC, Teufel M, Haußinger M, Enck P, Zipfel S (2011) Attentional processing of food pictures in individuals

with anorexia nervosa--an eye-tracking study. *Biol Psychiatry*, 69: 661-7.

34. Cheval B, Radel R, Neva JL, et al. (2018) Behavioral and Neural Evidence of the Rewarding Value of Exercise Behaviors: A Systematic Review. *Sports Med.* 48: 1389-404.

35. Fairburn CG (2008) *Cognitive Behavior Therapy and Eating Disorders*. New York: Guilford Press

36. Dalle Grave R (2008) Excessive and Compulsive Exercise in Eating Disorders: Prevalence, Associated Features, and Management. *Directions in Psychiatry*. 28(21)

37. Bechara A, Damasio AR, Damasio H, Anderson SW (1994) Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, 50: 7-15.

38. Beck AT, Steer RA, Ball R, Ranieri W (1996) Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess*, 67: 588-97.

39. Sanavio E (1988) Obsessions and compulsions: The Padua Inventory. *Behav Res Ther*, 26: 169-77.

40. Garner DM (1991) (EDI-2. *Eating Disorder Inventory-2*. Professional Manual Psychological Assessment Resource Inc.: Odessa, FL.

41. Spielberger CD (1983) *Manual for the State-Trait Inventory STAI (Form Y)*. Palo Alto, CA: Mind Garden.

42. Huijgen BC, Leemhuis S, Kok NM, et al (2015) Cognitive Functions in Elite and Sub-Elite Youth Soccer Players Aged 13 to 17 Years. *PLoS One*, 10: e0144580.

43. Winter B, Breitenstein C, Mooren FC, et al. (2007) High impact running improves learning. *Neurobiol Learn Mem* 2007, 87: 597-609.

44. Zach S & Shalom E (2016) The Influence of Acute Physical Activity on Working Memory. *Percept Mot Skills*, 122: 365-74.

45. Billeci L, Brunori E, Scardigli S, et al. (2018) Excessive physical activity in young girls with restrictive-type anorexia nervosa: its role on cardiac structure and performance. *Eat Weight Disord*, 23: 653-63.

46. Dalle Grave R, Calugi S, Marchesini G (2008) Is amenorrhea a clinically useful criterion for the diagnosis of anorexia nervosa? *Behav Res Ther*, 46: 1290-4.

47. Fairburn CG, Cooper Z, Doll HA, et al (2009) Transdiagnostic cognitive-behavioral therapy for patients with eating disorders: a two-site trial with 60-week follow-up. *Am J Psychiatry*, 166: 311-9.

48. Grau A, Magallón-Neri E, Faus G, Feixas G (2019) Cognitive impairment in eating disorder patients of short and long-term duration: a case-control study. *Neuropsychiatric disease and treatment*, 15: 1329-41.

49. Vassileva J, Gonzalez R, Bechara A, Martin EM (2007) Are all drug addicts impulsive? Effects of antisociality and extent of multi-drug use on cognitive and motor impulsivity. *Addict Behav*, 32: 3071-6.