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A Comparison of Auto Train Brain Neurofeedback Rewarding Interfaces in Terms of Efficacy

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ABSTRACT

Background/aim: Auto Train Brain is a mobile app that was specifically developed for dyslexic children to increase their reading speed and reading comprehension. In the original mobile app, only one unique neurofeedback user interface provided visually and audibly rewarding feedback to the subject with a red-green colored arrow on the screen. Later, new modules are added to the app with the end-users requests. These are the "youtube" video-based interface and "Spotify" auditory-based interface. In this research, we have compared the efficacy of the neurofeedback rewarding interfaces.

Materials and methods: The experiment group consists of 20 dyslexic children aged 7-to 10 (15 males, 5 females) who were randomly assigned to one rewarding interface and used it at home for more than six months.

Results: The result indicates that though the "youtube" interface is liked most by the participants, the arrow-based simple neurofeedback interface reduces theta brain waves more than other rewarding schemes. On the other hand, "youtube" and "Spotify" based interfaces increase Beta band powers more than the arrow interfaces in the cortex. The "Spotify" user interface improves the fast brain waves more on the temporal lobes (T7 and T8) as the feedback given was only auditory.

Conclusion: The results indicate that the relevant neurofeedback rewarding interface should be chosen based on the dyslexic child's specific condition.

Keywords: Neurofeedback, multimodality, QEEG, Auto Train Brain.

Auto Train Brain nörogeribildirim ödüllendirme arayüzlerinin etkinlik açısından karşılaştırılması

ÖZET

Arka plan/amaç: Auto Train Brain, disleksili çocukların okuma hızını ve anlama düzeyini artırmak için özel olarak geliştirilmiş bir mobil uygulamadır. Orijinal mobil uygulamada, yalnızca bir benzersiz nörogeribildirim kullanıcı arayüzü, ekranın kırmızı-yeşil renkli bir oku ile konuya görsel ve işitsel olarak ödüllendirici geri bildirimi sağlıyordu. Daha sonra, kullanıcı talepleriyle uygulamaya yeni modüller eklendi. Bunlar "youtube" video tabanlı arayüz ve "Spotify" işitsel tabanlı arayüzdür. Bu araştırmada, nörogeribildirim ödüllendirme arayüzlerinin etkinliğini karşılaştırdık.

Malzemeler ve yöntemler: Deney grubu, 6 ay ve üzeri süreyle evde bir ödüllendirme arayüzü kullanan ve 7 ila 10 yaş arasında (15 erkek, 5 kadın) disleksili çocuktan oluşmaktadır.

Sonuçlar: Sonuçlar, "youtube" arayüzünün katılımcılar tarafından en çok beğenilmesine rağmen, ok şeklindeki basit nörogeribildirim arayüzüne göre daha az theta beyin dalgaları azalttığını göstermektedir. Diğer yandan, "youtube" ve "Spotify" tabanlı arayüzler, kortekste ok arayüzlerinden daha fazla beta bant güçlerini artırmaktadır. "Spotify" kullanıcı arayüzü, sadece işitsel olarak verilen geri bildirim nedeniyle temporal loblarda (T7 ve T8) hızlı beyin dalgalarını daha da iyileştirir.

Çalışmanın özeti: Sonuçlar, disleksili çocuğun özel durumuna göre ilgili nörogeribildirim ödüllendirme arayüzünün seçilmesi gerektiğini göstermektedir.

Anahtar kelimeler: Nörogeribildirim, çoklu duyusal, QEEG, Auto Train Brain.

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Even if their IQ is normal or above average, some children may struggle to learn to read quickly in the early years of school. According to DSM-V criteria, dyslexia is a subtype of a distinct learning disability that affects children for at least 6 months and cannot be related to neurological or motor disorders, developmental disorders, or intellectual disabilities(1).

In dyslexia, neurologically, there is a temporal disruption and a disconnection between the left anterior and the left posterior regions of the brain (2). This situation affects the learning of letters and words and phonemic awareness. The increased slow brain waves in the left temporal region can be tracked in QEEG (3). The main affected brain region due to this disconnection syndrome might be the Wernicke region (4).

Neurofeedback has been shown to help with dyslexia's disconnection syndrome. Neurofeedback is beneficial in improving spelling, reading speed, and reading comprehension in studies (5,6,7,8). Neurofeedback employs the brain's plasticity and operant conditioning to teach the user how to gain greater control over central nervous system activity. The user receives direct neurofeedback regarding their actual brain activation pattern, allowing them to learn to control QEEG signals voluntarily (9). Real-time feedback of QEEG signals to oneself is a technique that allows individuals to obtain immediate feedback on their neural activity as reflected in visual and aural stimuli. It is a well-known reality that the neurons that fire together wire together (10).

Nazari used neurofeedback to decrease slow brain waves, such as delta and theta, at T3 and F7, while increasing beta-1 at T3 and F7(10). The treatment lowered the amount of time spent reading and the number of errors made while reading. Walker and Norman (5) used various neurofeedback protocols to reduce slow brain waves, such as delta and theta at Cz, enhance beta-1 at T3, and decrease coherence in the delta and theta range, and their findings revealed at least two levels of improvement in dyslexic reading levels. Applying neurofeedback to dyslexia (delta down at T3-T4, beta down at F7 and C3, coherence training in the delta, alpha, and beta regions) was shown to be beneficial for spelling but not reading (6). The latest research found that neurofeedback improves reading comprehension and reading speed (8).

Auto Train Brain is a mobile software that combines neurofeedback, multi-sensory learning, and special education principles (11,12,13). Machine learning algorithms exist for diagnosing dyslexia and recommending individualized treatment plans.

In Auto Train Brain's original user interface, there was a colored arrow to give neurofeedback to the child with a visual and auditory cue. Although it was simple and unique, this user interface was proven to be beneficial to children with dyslexia to improve their condition. During its product lifecycle, new features are added to Auto Train Brain. The neurofeedback interface is also developed more. In the latest version of Auto Train Brain, it is possible to choose the user's preferred video and start neurofeedback by providing multimodal -namely visually and audibly rewarding neurofeedback. When the subject focuses more on the video, he can see the screen more and can hear the sound of the video more. In another auditory rewarding scheme, the user starts a podcast or a storyteller on Spotify and runs in the background, while neurofeedback rewards the user by increasing or decreasing the volume of the sound.

In this research, we have collected QEEG data from children with dyslexia during neurofeedback sessions and determined which user interface decreased Theta brain waves more (5).

Materials and Methods

Subjects & Experimental Data

The neurofeedback data of 20 dyslexic children for 6 months are studied in this study. The children's ages range from seven to ten (15 males, 5 females). All participants gave their informed consent before the experiment after the experimental technique was explained to them according to research ethics committee requirements. The EMOTIV EPOC-X headset is used throughout the studies. The headset's internal sampling rate is 2048 samples per second per channel. The data is filtered to remove major artifacts before being downsampled to 128 samples per second per channel.

There are 14 EEG channels and two reference channels in total. Before the studies, the EMOTIV Headset is calibrated on the subjects' scalps using the EMOTIV APP, and each electrode is checked for high-quality EEG data transmission. The EEG electrode placements are AF3, F3, F7, FC5, T7, P7, O1, O2, P8, T8, FC6, F8, F4, and AF4.

The participants were randomly assigned the neurofeedback rewarding interfaces at the start of the experiment. The randomly assigned experiment groups were age-matched. Each group has only used the assigned rewarding interface. One group utilized a simple neurofeedback interface based on arrows. Their goal was to change the red arrow into a green arrow while avoiding hearing any beeps. The second group used the "youtube" interface, and the subject was told that if he focused more on the video, he would be able to view it better. The third group used the Spotify user interface. They listened to podcasts and when they give attention more, they can hear it better. The subjects were not given any extra information regarding the experimental technique.

Study Design

Each participant has used Auto Train for 6 months, has their brain waves read using the EMOTIV EPOC-X from 14 channels, and has received 30 minutes of visual and audio neurofeedback. The user interfaces for each group were different, but the neurofeedback algorithms were the same.

A recording of their QEEG is made and stored in a database. All 14-channel QEEG data is acquired during the tests in the Theta (4-8 Hz), Alpha (8-12 Hz), Beta-1 (12-16 Hz), Beta-2 (1625 Hz), and Gamma (25-45 Hz) bands for all analyses in this work. We evaluated the Theta band power values for 14 channels after collecting, averaging, and cleaning data from an EMOTIV EPOC-X headset.

Results

It was measured that the simple "arrow" based neurofeedback interface, which rewards visually and audibly, decreases theta band power more than that of the other neurofeedback interfaces ($p<.001$).

It was also measured that "youtube" and "Spotify" based neurofeedback rewarding interfaces improve Beta-1 and Beta-2 brain waves more than the arrow neurofeedback rewarding interface ($p<0.001$). There is no comparison between the improvements in reading comprehension / reading speed and neurofeedback interfaces.

Discussion

We have designed an experiment to test the new user interfaces of Auto Train Brain. The first neurofeedback interface is related to the "arrow" neurofeedback interface which is simply turning a red arrow into a green arrow. The second neurofeedback interface is related to "youtube" videos and neurofeedback during watching these videos. The third neurofeedback interface was based on Spotify (storyteller), an auditory interface. The users of Auto Train Brain prefer the "youtube" videos more than the "arrow" interface in real life as they think it is more amusing and attractive. The results of this experiment have shown that the original "arrow" interface which is easier to control and learn was more beneficial to children with dyslexia to reduce the slow brain waves. The reason would be to control the "arrow" much easier than the "youtube videos" with the brain, or the content of the "youtube" videos were distracting the children to focus.

Participants used the "youtube" interface to pay more attention to cartoon movies and therefore their fast brain waves increased more. The "Spotify" user interface improves the fast brain waves more on the temporal lobes (T7 and T8) as the feedback given was only auditory. The results indicate that the relevant neurofeedback rewarding interface should be chosen based on the child's specific condition. Some dyslexic people have general slowing or focal slowing of the cortex. Some dyslexic people have left temporal disruption. If the aim is to reduce the slow brain waves in the cortex or the theta brain waves should be trained, then the arrow-based interface should be chosen. If the aim is to increase the Beta brain waves in the cortex, "youtube" and/or "Spotify" based neurofeedback interfaces should be chosen. If the aim is to train phonemic awareness or auditory comprehension, a "Spotify" based user interface should be chosen. There may be a placebo effect and maturation effect in the experiments.

Extreme qEEG readings have been shown to be more likely to return to normal readings following Live z-score neurofeedback, especially in those who had normal alpha peak frequencies prior to the trial (12). EEG-based BCI systems have the potential to improve many people's lives because they are so powerful (13). According to the study, games are primarily top-down designed with kids in mind. They are typically motivated by causes outside of neurodivergent interests and tend to concentrate on educational and medical contexts. The majority of current work adopts a medical paradigm of impairment, which fails to promote neurodivergent players' autonomy and limits their options for immersion (14).

Simple observation of particular items has the ability to activate motor neurons. Neural responses to objects can vary significantly depending on their characteristics, and there are currently no standards for designing brain-computer interfaces (15). Our research offers fresh perspectives that will soon improve BCI design.

Figure -1 *Auto Train Brain "arrow" interface*

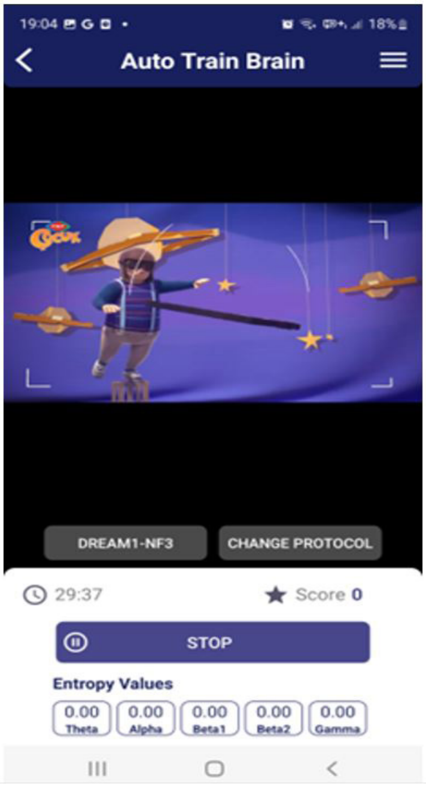

Figure -2 *Auto Train Brain "youtube" interface*

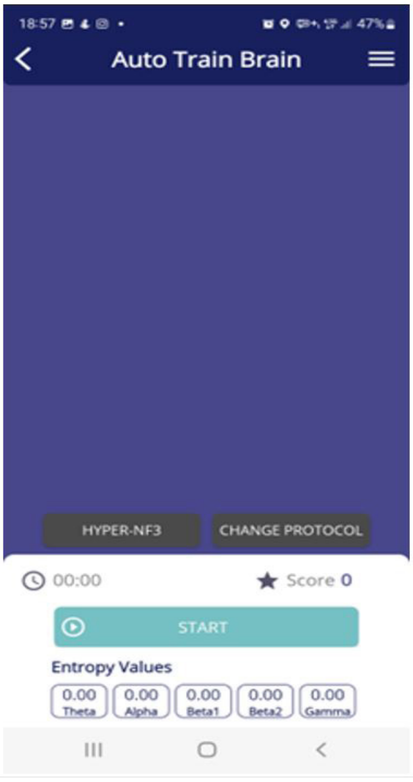

Figure -3 *Auto Train Brain "Spotify" interface*

Table 1. qEEG Band Power values per channel for each neurofeedback rewarding interface				
Variable	Youtube N = 382	Arrow N = 169	Spotify N = 104	p-Value
THETA_AF3	4.05 (± 2.96) 95% CI: [3.75 ; 4.35] Range: (0.0 ; 13.38) N = 382	3.73 (± 1.51) 95% CI: [3.5 ; 3.96] Range: (0.0 ; 8.73) N = 169	5.12 (± 2.97) 95% CI: [4.54 ; 5.69] Range: (0.0 ; 14.17) N = 104	<0.001
THETA_F3	4.61 (± 3.02) 95% CI: [4.3 ; 4.91] Range: (0.0 ; 13.84) N = 382	3.25 (± 1.3) 95% CI: [3.05 ; 3.44] Range: (0.0 ; 7.46) N = 169	5.26 (± 2.54) 95% CI: [4.76 ; 5.75] Range: (0.0 ; 13.41) N = 104	<0.001
THETA_F7	4.26 (± 2.4) 95% CI: [4.02 ; 4.5] Range: (0.0 ; 11.14) N = 382	3.47 (± 1.54) 95% CI: [3.23 ; 3.7] Range: (0.0 ; 9.1) N = 169	5.11 (± 1.9) 95% CI: [4.74 ; 5.48] Range: (0.165 ; 12.21) N = 104	<0.001
THETA_FC5	4.15 (± 2.11) 95% CI: [3.94 ; 4.36] Range: (0.0 ; 11.73) N = 382	2.93 (± 1.27) 95% CI: [2.74 ; 3.12] Range: (0.0 ; 6.87) N = 169	4.88 (± 2.34) 95% CI: [4.43 ; 5.34] Range: (0.0 ; 13.89) N = 104	<0.001
THETA_T7	3.05 (± 2.41) 95% CI: [2.81 ; 3.29] Range: (0.0 ; 12.75) N = 382	2.14 (± 1.28) 95% CI: [1.95 ; 2.34] Range: (0.0 ; 8.34) N = 169	3.23 (± 2.06) 95% CI: [2.83 ; 3.62] Range: (0.0264 ; 11.28) N = 104	<0.001
THETA_P7	2.52 (± 1.94) 95% CI: [2.33 ; 2.72] Range: (0.0 ; 14.06) N = 382	1.79 (± 1.14) 95% CI: [1.62 ; 1.96] Range: (0.00917 ; 6.72) N = 169	3.03 (± 1.92) 95% CI: [2.66 ; 3.4] Range: (0.149 ; 11.06) N = 104	<0.001
THETA_O1	3.72 (± 2.61) 95% CI: [3.46 ; 3.98] Range: (0.0 ; 14.51) N = 382	2.28 (± 1.07) 95% CI: [2.12 ; 2.45] Range: (0.0 ; 6.27) N = 169	4.4 (± 2.16) 95% CI: [3.98 ; 4.82] Range: (0.173 ; 13.39) N = 104	<0.001
THETA_O2	3.71 (± 2.22) 95% CI: [3.49 ; 3.94] Range: (0.0 ; 11.49) N = 382	2.58 (± 1.33) 95% CI: [2.38 ; 2.78] Range: (0.0 ; 7.27) N = 169	4.92 (± 2.5) 95% CI: [4.44 ; 5.41] Range: (0.198 ; 12.23) N = 104	<0.001
THETA_P8	3.17 (± 2.32) 95% CI: [2.93 ; 3.4] Range: (0.0 ; 11.59) N = 382	2.48 (± 1.72) 95% CI: [2.22 ; 2.74] Range: (0.0 ; 11.13) N = 169	3.94 (± 2.73) 95% CI: [3.41 ; 4.47] Range: (0.0 ; 11.77) N = 104	<0.001
THETA_T8	3.9 (± 2.22) 95% CI: [3.68 ; 4.12] Range: (0.0 ; 12.95) N = 382	3.03 (± 1.75) 95% CI: [2.77 ; 3.3] Range: (0.0 ; 8.39) N = 169	4.91 (± 2.49) 95% CI: [4.42 ; 5.39] Range: (0.14 ; 12.43) N = 104	<0.001
THETA_FC6	4.91 (± 2.92) 95% CI: [4.61 ; 5.2] Range: (0.0 ; 14.85) N = 382	4.16 (± 2.05) 95% CI: [3.85 ; 4.47] Range: (0.0 ; 13.16) N = 169	5.87 (± 2.79) 95% CI: [5.33 ; 6.41] Range: (0.0 ; 13.01) N = 104	<0.001
THETA_F8	5.34 (± 3.28) 95% CI: [5.01 ; 5.67] Range: (0.0 ; 14.36) N = 382	4.09 (± 1.86) 95% CI: [3.81 ; 4.37] Range: (0.0 ; 12.24) N = 169	5.92 (± 2.81) 95% CI: [5.37 ; 6.47] Range: (0.0 ; 12.79) N = 104	<0.001
THETA_F4	4.72 (± 2.8) 95% CI: [4.44 ; 5.0] Range: (0.0 ; 14.4) N = 382	4.18 (± 1.86) 95% CI: [3.9 ; 4.47] Range: (0.0 ; 10.34) N = 169	5.79 (± 2.13) 95% CI: [5.38 ; 6.2] Range: (0.0775 ; 12.48) N = 104	<0.001
THETA_AF4	5.02 (± 2.83) 95% CI: [4.74 ; 5.31] Range: (0.0 ; 12.5) N = 382	4.19 (± 1.86) 95% CI: [3.91 ; 4.47] Range: (0.0 ; 10.47) N = 169	5.58 (± 2.54) 95% CI: [5.08 ; 6.07] Range: (0.0 ; 12.8) N = 104	<0.001

ALPHA_AF3	2.6 (± 2.08) 95% CI: [2.39 ; 2.81] Range: (0.0 ; 8.47) N = 382	2.19 (± 1.68) 95% CI: [1.93 ; 2.44] Range: (0.0 ; 14.99) N = 169	3.69 (± 3.36) 95% CI: [3.04 ; 4.34] Range: (0.0 ; 15.64) N = 104	0.004
ALPHA_F3	3.67 (± 2.84) 95% CI: [3.38 ; 3.95] Range: (0.0 ; 12.84) N = 382	2.04 (± 1.51) 95% CI: [1.81 ; 2.27] Range: (0.0 ; 13.91) N = 169	4.71 (± 3.82) 95% CI: [3.96 ; 5.45] Range: (0.0 ; 15.38) N = 104	<0.001
ALPHA_F7	2.48 (± 1.6) 95% CI: [2.32 ; 2.64] Range: (0.0 ; 7.85) N = 382	1.88 (± 1.26) 95% CI: [1.69 ; 2.07] Range: (0.0 ; 9.8) N = 169	3.37 (± 2.09) 95% CI: [2.96 ; 3.78] Range: (0.142 ; 11.33) N = 104	<0.001
ALPHA_FC5	2.84 (± 1.69) 95% CI: [2.67 ; 3.01] Range: (0.0 ; 9.21) N = 382	1.74 (± 1.27) 95% CI: [1.55 ; 1.93] Range: (0.0 ; 10.17) N = 169	3.81 (± 2.79) 95% CI: [3.27 ; 4.36] Range: (0.0 ; 14.73) N = 104	<0.001
ALPHA_T7	2.05 (± 1.71) 95% CI: [1.88 ; 2.22] Range: (0.0 ; 12.12) N = 382	1.23 (± 0.887) 95% CI: [1.09 ; 1.36] Range: (0.0 ; 6.51) N = 169	2.3 (± 1.74) 95% CI: [1.96 ; 2.64] Range: (0.0188 ; 9.53) N = 104	<0.001
ALPHA_P7	1.83 (± 1.46) 95% CI: [1.68 ; 1.97] Range: (0.0 ; 13.93) N = 382	1.38 (± 1.26) 95% CI: [1.19 ; 1.57] Range: (0.0136 ; 12.74) N = 169	2.77 (± 2.6) 95% CI: [2.27 ; 3.28] Range: (0.175 ; 18.65) N = 104	<0.001
ALPHA_O1	3.39 (± 2.17) 95% CI: [3.17 ; 3.61] Range: (0.0 ; 15.62) N = 382	2.86 (± 2.81) 95% CI: [2.44 ; 3.29] Range: (0.0 ; 20.38) N = 169	5.79 (± 3.76) 95% CI: [5.06 ; 6.52] Range: (0.24 ; 18.5) N = 104	<0.001
ALPHA_O2	3.54 (± 2.4) 95% CI: [3.3 ; 3.78] Range: (0.0 ; 10.38) N = 382	2.71 (± 1.81) 95% CI: [2.43 ; 2.98] Range: (0.0 ; 8.27) N = 169	5.73 (± 3.65) 95% CI: [5.02 ; 6.44] Range: (0.247 ; 17.39) N = 104	<0.001
ALPHA_P8	2.86 (± 2.36) 95% CI: [2.62 ; 3.1] Range: (0.0 ; 10.12) N = 382	2.11 (± 1.54) 95% CI: [1.88 ; 2.34] Range: (0.0 ; 7.75) N = 169	3.9 (± 3.41) 95% CI: [3.24 ; 4.57] Range: (0.0 ; 14.29) N = 104	<0.001
ALPHA_T8	3.6 (± 2.41) 95% CI: [3.36 ; 3.84] Range: (0.0 ; 10.69) N = 382	2.32 (± 1.78) 95% CI: [2.05 ; 2.59] Range: (0.0 ; 8.75) N = 169	4.74 (± 3.64) 95% CI: [4.03 ; 5.45] Range: (0.18 ; 16.75) N = 104	<0.001
ALPHA_FC6	4.15 (± 2.91) 95% CI: [3.86 ; 4.44] Range: (0.0 ; 12.21) N = 382	2.95 (± 2.49) 95% CI: [2.57 ; 3.33] Range: (0.0 ; 24.05) N = 169	5.64 (± 4.46) 95% CI: [4.77 ; 6.5] Range: (0.0 ; 17.0) N = 104	<0.001
ALPHA_F8	4.41 (± 3.19) 95% CI: [4.09 ; 4.74] Range: (0.0 ; 13.12) N = 382	3.05 (± 2.98) 95% CI: [2.6 ; 3.5] Range: (0.0 ; 29.34) N = 169	6.08 (± 4.9) 95% CI: [5.13 ; 7.04] Range: (0.0 ; 21.75) N = 104	<0.001
ALPHA_F4	3.34 (± 2.3) 95% CI: [3.11 ; 3.57] Range: (0.0 ; 9.81) N = 382	2.64 (± 1.93) 95% CI: [2.34 ; 2.93] Range: (0.0 ; 12.82) N = 169	4.7 (± 3.15) 95% CI: [4.09 ; 5.32] Range: (0.0808 ; 13.99) N = 104	<0.001
ALPHA_AF4	3.74 (± 2.44) 95% CI: [3.49 ; 3.98] Range: (0.0 ; 10.34) N = 382	2.71 (± 2.26) 95% CI: [2.36 ; 3.05] Range: (0.0 ; 18.22) N = 169	4.58 (± 3.48) 95% CI: [3.9 ; 5.26] Range: (0.0 ; 15.24) N = 104	<0.001
BETA1_AF3	1.68 (± 1.5) 95% CI: [1.53 ; 1.83] Range: (0.0 ; 11.56) N = 382	1.36 (± 0.92) 95% CI: [1.22 ; 1.5] Range: (0.0 ; 7.19) N = 169	2.08 (± 1.86) 95% CI: [1.72 ; 2.44] Range: (0.0 ; 9.31) N = 104	0.04

BETA1_F3	2.28 (± 1.88) 95% CI: [2.09 ; 2.47] Range: (0.0 ; 11.83) N = 382	1.28 (± 0.862) 95% CI: [1.15 ; 1.42] Range: (0.0 ; 6.84) N = 169	2.67 (± 2.02) 95% CI: [2.28 ; 3.07] Range: (0.0 ; 8.92) N = 104	<0.001
BETA1_F7	1.54 (± 1.11) 95% CI: [1.43 ; 1.65] Range: (0.0 ; 6.77) N = 382	1.2 (± 0.853) 95% CI: [1.07 ; 1.33] Range: (0.0 ; 7.29) N = 169	1.88 (± 1.31) 95% CI: [1.63 ; 2.14] Range: (0.0787 ; 7.93) N = 104	<0.001
BETA1_FC5	1.85 (± 1.22) 95% CI: [1.73 ; 1.97] Range: (0.0 ; 7.35) N = 382	1.2 (± 0.805) 95% CI: [1.08 ; 1.32] Range: (0.0 ; 7.19) N = 169	2.21 (± 1.54) 95% CI: [1.91 ; 2.51] Range: (0.0 ; 8.44) N = 104	<0.001
BETA1_T7	1.75 (± 1.58) 95% CI: [1.59 ; 1.91] Range: (0.0 ; 13.06) N = 382	0.947 (± 0.725) 95% CI: [0.837 ; 1.06] Range: (0.0 ; 5.12) N = 169	1.56 (± 1.23) 95% CI: [1.32 ; 1.8] Range: (0.0138 ; 6.57) N = 104	<0.001
BETA1_P7	1.41 (± 1.29) 95% CI: [1.28 ; 1.54] Range: (0.0 ; 12.61) N = 382	1.2 (± 1.24) 95% CI: [1.01 ; 1.39] Range: (0.0109 ; 12.45) N = 169	2.1 (± 2.63) 95% CI: [1.59 ; 2.61] Range: (0.107 ; 19.19) N = 104	<0.001
BETA1_O1	2.22 (± 1.7) 95% CI: [2.05 ; 2.39] Range: (0.0 ; 13.41) N = 382	2.38 (± 2.66) 95% CI: [1.97 ; 2.78] Range: (0.0 ; 14.25) N = 169	3.49 (± 2.73) 95% CI: [2.95 ; 4.02] Range: (0.0965 ; 16.92) N = 104	<0.001
BETA1_O2	2.09 (± 1.59) 95% CI: [1.93 ; 2.25] Range: (0.0 ; 10.17) N = 382	2.08 (± 2.23) 95% CI: [1.74 ; 2.42] Range: (0.0 ; 23.75) N = 169	3.37 (± 2.21) 95% CI: [2.94 ; 3.8] Range: (0.131 ; 13.95) N = 104	<0.001
BETA1_P8	1.84 (± 1.53) 95% CI: [1.69 ; 2.0] Range: (0.0 ; 10.06) N = 382	1.68 (± 1.47) 95% CI: [1.46 ; 1.91] Range: (0.0 ; 14.14) N = 169	2.34 (± 1.63) 95% CI: [2.02 ; 2.66] Range: (0.0 ; 6.76) N = 104	0.002
BETA1_T8	2.52 (± 1.82) 95% CI: [2.34 ; 2.7] Range: (0.0 ; 12.11) N = 382	1.74 (± 1.28) 95% CI: [1.55 ; 1.94] Range: (0.0 ; 8.1) N = 169	2.92 (± 2.09) 95% CI: [2.51 ; 3.32] Range: (0.1 ; 9.58) N = 104	<0.001
BETA1_FC6	2.74 (± 2.01) 95% CI: [2.54 ; 2.95] Range: (0.0 ; 12.12) N = 382	2.04 (± 1.47) 95% CI: [1.81 ; 2.26] Range: (0.0 ; 10.86) N = 169	3.26 (± 2.2) 95% CI: [2.84 ; 3.69] Range: (0.0 ; 11.28) N = 104	<0.001
BETA1_F8	3.05 (± 2.4) 95% CI: [2.81 ; 3.29] Range: (0.0 ; 13.71) N = 382	2.07 (± 1.59) 95% CI: [1.83 ; 2.31] Range: (0.0 ; 11.13) N = 169	3.61 (± 2.49) 95% CI: [3.12 ; 4.09] Range: (0.0 ; 11.97) N = 104	<0.001
BETA1_F4	2.15 (± 1.63) 95% CI: [1.99 ; 2.31] Range: (0.0 ; 9.61) N = 382	1.69 (± 1.21) 95% CI: [1.5 ; 1.87] Range: (0.0 ; 9.66) N = 169	2.59 (± 1.65) 95% CI: [2.27 ; 2.91] Range: (0.0446 ; 10.28) N = 104	<0.001
BETA1_AF4	2.55 (± 1.87) 95% CI: [2.36 ; 2.74] Range: (0.0 ; 13.6) N = 382	1.73 (± 1.23) 95% CI: [1.54 ; 1.91] Range: (0.0 ; 8.68) N = 169	2.71 (± 1.89) 95% CI: [2.35 ; 3.08] Range: (0.0 ; 10.78) N = 104	<0.001
BETA2_AF3	1.02 (± 1.15) 95% CI: [0.902 ; 1.13] Range: (0.0 ; 12.01) N = 382	0.906 (± 1.01) 95% CI: [0.753 ; 1.06] Range: (0.0 ; 8.61) N = 169	1.17 (± 1.45) 95% CI: [0.887 ; 1.45] Range: (0.0 ; 12.91) N = 104	0.167
BETA2_F3	1.03 (± 0.924) 95% CI: [0.932 ; 1.12] Range: (0.0 ; 6.92) N = 382	0.82 (± 0.911) 95% CI: [0.681 ; 0.958] Range: (0.0 ; 7.63) N = 169	1.19 (± 1.32) 95% CI: [0.936 ; 1.45] Range: (0.0 ; 12.44) N = 104	<0.001

BETA2_F7	1.0 (± 0.861) 95% CI: [0.915 ; 1.09] Range: (0.0 ; 5.77) N = 382	0.848 (± 1.08) 95% CI: [0.684 ; 1.01] Range: (0.0 ; 9.74) N = 169	1.16 (± 1.15) 95% CI: [0.939 ; 1.39] Range: (0.0426 ; 10.94) N = 104	<0.001
BETA2_FC5	1.24 (± 0.967) 95% CI: [1.15 ; 1.34] Range: (0.0 ; 6.53) N = 382	0.884 (± 1.04) 95% CI: [0.726 ; 1.04] Range: (0.0 ; 9.09) N = 169	1.36 (± 1.32) 95% CI: [1.11 ; 1.62] Range: (0.0 ; 12.24) N = 104	<0.001
BETA2_T7	1.96 (± 2.8) 95% CI: [1.68 ; 2.24] Range: (0.0 ; 34.69) N = 382	0.783 (± 1.0) 95% CI: [0.631 ; 0.935] Range: (0.0 ; 9.13) N = 169	1.15 (± 1.15) 95% CI: [0.932 ; 1.38] Range: (0.0101 ; 9.36) N = 104	<0.001
BETA2_P7	1.15 (± 2.14) 95% CI: [0.937 ; 1.37] Range: (0.0 ; 35.47) N = 382	0.996 (± 1.31) 95% CI: [0.798 ; 1.19] Range: (0.00794 ; 9.63) N = 169	1.37 (± 1.45) 95% CI: [1.09 ; 1.65] Range: (0.0487 ; 9.88) N = 104	<0.001
BETA2_O1	1.17 (± 1.03) 95% CI: [1.06 ; 1.27] Range: (0.0 ; 7.0) N = 382	1.41 (± 1.53) 95% CI: [1.18 ; 1.65] Range: (0.0 ; 9.19) N = 169	1.86 (± 1.58) 95% CI: [1.55 ; 2.17] Range: (0.0373 ; 8.92) N = 104	<0.001
BETA2_O2	1.11 (± 1.04) 95% CI: [1.0 ; 1.21] Range: (0.0 ; 8.06) N = 382	1.14 (± 1.0) 95% CI: [0.984 ; 1.29] Range: (0.0 ; 7.92) N = 169	1.74 (± 1.23) 95% CI: [1.5 ; 1.98] Range: (0.0525 ; 8.42) N = 104	<0.001
BETA2_P8	1.12 (± 1.14) 95% CI: [1.01 ; 1.24] Range: (0.0 ; 9.33) N = 382	1.15 (± 1.12) 95% CI: [0.98 ; 1.32] Range: (0.0 ; 7.74) N = 169	1.43 (± 1.03) 95% CI: [1.23 ; 1.63] Range: (0.0 ; 4.78) N = 104	0.002
BETA2_T8	2.13 (± 3.08) 95% CI: [1.82 ; 2.44] Range: (0.0 ; 32.41) N = 382	1.17 (± 1.14) 95% CI: [1.0 ; 1.35] Range: (0.0 ; 9.06) N = 169	2.07 (± 1.99) 95% CI: [1.69 ; 2.46] Range: (0.0387 ; 12.37) N = 104	<0.001
BETA2_FC6	1.56 (± 1.43) 95% CI: [1.41 ; 1.7] Range: (0.0 ; 9.61) N = 382	2.67 (± 12.02) 95% CI: [0.846 ; 4.5] Range: (0.0 ; 139.5) N = 169	1.82 (± 1.72) 95% CI: [1.48 ; 2.15] Range: (0.0 ; 16.0) N = 104	0.002
BETA2_F8	1.38 (± 1.34) 95% CI: [1.25 ; 1.52] Range: (0.0 ; 11.04) N = 382	2.47 (± 12.53) 95% CI: [0.572 ; 4.38] Range: (0.0 ; 148.74) N = 169	1.69 (± 1.78) 95% CI: [1.34 ; 2.03] Range: (0.0 ; 16.89) N = 104	0.004
BETA2_F4	1.27 (± 1.14) 95% CI: [1.16 ; 1.39] Range: (0.0 ; 7.96) N = 382	1.22 (± 1.83) 95% CI: [0.944 ; 1.5] Range: (0.0 ; 19.05) N = 169	1.55 (± 1.55) 95% CI: [1.25 ; 1.85] Range: (0.0226 ; 14.88) N = 104	<0.001
BETA2_AF4	1.39 (± 1.77) 95% CI: [1.21 ; 1.57] Range: (0.0 ; 20.79) N = 382	1.37 (± 3.02) 95% CI: [0.908 ; 1.83] Range: (0.0 ; 34.27) N = 169	1.43 (± 1.56) 95% CI: [1.12 ; 1.73] Range: (0.0 ; 15.05) N = 10	0.006
GAMMA_AF3	0.868 (± 1.46) 95% CI: [0.721 ; 1.01] Range: (0.0 ; 20.52) N = 382	0.774 (± 1.31) 95% CI: [0.576 ; 0.973] Range: (0.0 ; 11.27) N = 169	1.08 (± 2.21) 95% CI: [0.646 ; 1.5] Range: (0.0 ; 21.7) N = 104	0.097
GAMMA_F3	0.724 (± 0.892) 95% CI: [0.634 ; 0.814] Range: (0.0 ; 7.56) N = 382	0.727 (± 1.49) 95% CI: [0.501 ; 0.953] Range: (0.0 ; 13.5) N = 169	0.992 (± 2.09) 95% CI: [0.586 ; 1.4] Range: (0.0 ; 21.18) N = 104	0.002
GAMMA_F7	0.774 (± 0.851) 95% CI: [0.689 ; 0.86] Range: (0.0 ; 7.73) N = 382	0.745 (± 1.36) 95% CI: [0.538 ; 0.952] Range: (0.0 ; 12.52) N = 169	1.06 (± 1.78) 95% CI: [0.715 ; 1.41] Range: (0.0224 ; 17.83) N = 104	<0.001

GAMMA_FC5	0.966 (± 0.941) 95% CI: [0.872 ; 1.06] Range: (0.0 ; 7.33) N = 382	0.815 (± 1.46) 95% CI: [0.593 ; 1.04] Range: (0.0 ; 12.9) N = 169	1.22 (± 2.06) 95% CI: [0.816 ; 1.62] Range: (0.0 ; 20.67) N = 104	<0.001
GAMMA_T7	1.61 (± 2.97) 95% CI: [1.32 ; 1.91] Range: (0.0 ; 41.77) N = 382	0.746 (± 1.2) 95% CI: [0.565 ; 0.928] Range: (0.0 ; 10.02) N = 169	1.14 (± 1.75) 95% CI: [0.799 ; 1.48] Range: (0.00463 ; 16.1) N = 104	<0.001
GAMMA_P7	0.882 (± 1.11) 95% CI: [0.771 ; 0.994] Range: (0.0 ; 9.39) N = 382	0.923 (± 1.3) 95% CI: [0.726 ; 1.12] Range: (0.00246 ; 9.77) N = 169	1.26 (± 1.55) 95% CI: [0.958 ; 1.56] Range: (0.0284 ; 9.33) N = 104	<0.001
GAMMA_O1	0.923 (± 1.05) 95% CI: [0.817 ; 1.03] Range: (0.0 ; 7.28) N = 382	1.52 (± 3.48) 95% CI: [0.992 ; 2.05] Range: (0.0 ; 41.68) N = 169	1.66 (± 1.94) 95% CI: [1.28 ; 2.04] Range: (0.0175 ; 15.62) N = 104	<0.001
GAMMA_O2	0.851 (± 1.04) 95% CI: [0.746 ; 0.956] Range: (0.0 ; 9.69) N = 382	1.02 (± 1.31) 95% CI: [0.826 ; 1.22] Range: (0.0 ; 11.78) N = 169	1.51 (± 1.69) 95% CI: [1.19 ; 1.84] Range: (0.0244 ; 15.03) N = 104	<0.001
GAMMA_P8	0.852 (± 1.07) 95% CI: [0.744 ; 0.96] Range: (0.0 ; 10.96) N = 382	1.11 (± 1.5) 95% CI: [0.879 ; 1.34] Range: (0.0 ; 11.11) N = 169	1.24 (± 1.21) 95% CI: [1.01 ; 1.48] Range: (0.0 ; 8.97) N = 104	<0.001
GAMMA_T8	1.6 (± 2.35) 95% CI: [1.36 ; 1.83] Range: (0.0 ; 26.29) N = 382	1.52 (± 6.7) 95% CI: [0.498 ; 2.53] Range: (0.0 ; 86.04) N = 169	2.01 (± 2.69) 95% CI: [1.48 ; 2.53] Range: (0.0167 ; 20.99) N = 104	<0.001
GAMMA_FC6	1.19 (± 1.47) 95% CI: [1.04 ; 1.33] Range: (0.0 ; 13.17) N = 382	1.46 (± 3.42) 95% CI: [0.942 ; 1.98] Range: (0.0 ; 37.29) N = 169	1.61 (± 2.86) 95% CI: [1.06 ; 2.17] Range: (0.0 ; 28.77) N = 104	<0.001
GAMMA_F8	1.0 (± 1.4) 95% CI: [0.86 ; 1.14] Range: (0.0 ; 14.62) N = 382	3.23 (± 23.79) 95% CI: [-0.386 ; 6.84] Range: (0.0 ; 303.08) N = 169	1.44 (± 2.91) 95% CI: [0.876 ; 2.01] Range: (0.0 ; 29.42) N = 104	0.003
GAMMA_F4	0.974 (± 1.22) 95% CI: [0.851 ; 1.1] Range: (0.0 ; 10.98) N = 382	1.27 (± 3.73) 95% CI: [0.703 ; 1.84] Range: (0.0 ; 36.68) N = 169	1.41 (± 2.53) 95% CI: [0.922 ; 1.91] Range: (0.00952 ; 25.11) N = 104	<0.001
GAMMA_AF4	1.03 (± 1.48) 95% CI: [0.881 ; 1.18] Range: (0.0 ; 13.61) N = 382	1.59 (± 6.76) 95% CI: [0.565 ; 2.62] Range: (0.0 ; 79.33) N = 169	1.27 (± 2.57) 95% CI: [0.766 ; 1.77] Range: (0.0 ; 25.54) N = 104	0.015

DECLARATIONS

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Informed Consent: All the participants gave their informed consent after the experimental procedure was explained to them by guidelines set by the research ethics committee of Sabancı University, the protocol of the study was approved by the Ethics Committee of Yeditepe University and the clinical trial was registered to the Turkey Pharmaceuticals and Medical Devices Agency (Nbr: 71146310-511.06,2.11.2018).

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