

As a manuscript

Khayrullina Guzal Maratovna

**Features of executive functions in obsessive-compulsive disorder:
psychophysiological study**

Summary
of the dissertation for the purpose of obtaining academic degree
Doctor of Philosophy in Cognitive Sciences

Academic supervisor:
PhD, Martynova Olga Vladimirovna

Table of contents

1. INTRODUCTION	4
1.1. Research problem and its significance	4
1.2. Hypotheses, goals and objectives of the study	6
1.3. Theoretical and methodological justification	7
1.3.1. Theoretical background	7
1.3.2. Research methodology.....	11
1.4. Scientific novelty	13
1.4.1. Theoretical novelty	13
1.4.2. Methodological novelty	14
1.5. Theoretical and practical significance	14
1.6. Provisions for the defense.....	15
1.7. Author Contribution.....	15
2. DESCRIPTION OF THE STUDIES	16
2.1. Study I. Features of oculomotor reactions in highly anxious volunteers with different level of impulsivity in solving different types of the antisaccade task.	16
2.2. Study II. Increased error rate and delayed response to negative emotional stimuli in antisaccade task in obsessive-compulsive disorder.....	23
2.3. Study III. Dynamics of the autonomic nervous system during cognitive-emotional load in obsessive-compulsive disorder	28
3. CONCLUSION	36
REFERENCES	38

The work was carried out in the Center for Neuroeconomics and Cognitive Research of the National Research University Higher School of Economics.

The main results of the dissertation research are presented in the following publications:

1. **Khayrullina G.M.**, Panfilova E.A., Martynova O.V. (2023). Features of oculomotor reactions in highly anxious volunteers with different level of impulsivity in solving different types of the antisaccade task. *I.P. Pavlov Journal of Higher Nervous Activity*, 73 (3), 411-424. DOI: 10.31857/S0044467723030085.
2. **Khayrullina G.**, Panfilova E., Martynova O. (2023). Increased error rate and delayed response to negative emotional stimuli in antisaccade task in obsessive-compulsive disorder. *International Journal of Psychophysiology*, 192, 62-71. DOI: 10.1016/j.ijpsycho.2023.08.009.
3. Portnova G., **Khayrullina G.**, Martynova O. (2024). Temporal dynamics of autonomic nervous system responses under cognitive-emotional workload in obsessive-compulsive disorder. *Psychophysiology*, 00, e14549. DOI: 10.1111/psyp.1454.

Other publications:

1. Khayrullina G.M., Moiseeva V.V., Martynova O.V. (2022). Specific Aspects of Eye movement Reactions as Markers of Cognitive Control disorders in Patients with Obsessive-Compulsive Disorder (Review). *Modern technologies in medicine*, 14(2), 80-98. DOI: 10.17691/stm2022.14.2.08.

Selected scientific conferences where the results were presented:

- I.A. Shevelev conference on the physiology of sensory systems, Moscow, Russia, 2022;
- 24th Congress of the Physiological Society named after. I.P. Pavlov, St. Petersburg, Russia, 2023;
- 23 World Congress of Psychiatry, Vienna, Austria, 2023.

1. INTRODUCTION

1.1. Research problem and its significance

Obsessive-compulsive disorder (OCD) is one of the most disabling mental illnesses, according to the World Health Organization (WHO, 1999). OCD, according to ICD-10 and ICD-11, is characterized by the presence of persistent intrusive thoughts and/or repetitive compulsive behaviors (WHO, 2019; WHO, 2022). Intrusive thoughts are ideas, images, or impulses that repeatedly appear in a person's mind and which he cannot get rid of. It is important to note that, even though these thoughts are involuntary and often disgusting, people with OCD recognize them as their own. Compulsive actions, or rituals, are stereotyped behaviors that are repeated over and over again. They do not bring pleasure or serve a useful purpose, but rather are a means of relieving the anxiety associated with preventing unlikely events. Patients with OCD avoid situations that cause discomfort, even if there is no real threat. This behavior can lead to limited social contacts and a deterioration in the quality of life, as well as have a negative impact on the socio-economic sphere of society as a whole. Many people with OCD do not seek help for many years due to stigma, despite understanding that obsessive thoughts are meaningless and/or rituals are ineffective (Fineberg et al., 2018; Nakao et al., 2014; WHO, 1983, 2022).

Despite the expansion of scientific knowledge about OCD, a number of questions about the psychophysiological features of this disease remain unresolved. Clinical manifestations of OCD include the inability to stop recurring negative thoughts, avoid unhelpful activities, and shift attention to more productive activities. Neuropsychological studies in patients with OCD have identified deficits in executive functions, including impairments in inhibitory control and attention (Benzina et al., 2016). At the same time, unlike other disorders, patients with OCD retain the ability to self-criticize: patients suffering from this disorder are aware of the inadequacy, illogicality of their compulsive actions and the absurdity of obsessive thoughts, but cannot resist them.

OCD symptoms, however, are not limited to the inability to resist intrusive thoughts or actions, but also include increased anxiety. In addition to impairments

in inhibitory control and attention, patients with OCD may experience difficulty regulating emotions (Fernández De La Cruz et al., 2013; Stern & Taylor, 2014), which in turn may cause impairment in executive functioning (Bannon et al., 2008; Bohne et al., 2005). This can, in turn, lead to an inability to stop unnecessary thoughts and actions. For example, compulsions can be viewed as a maladaptive emotional regulation (ER) strategy that is used to alleviate psychological distress (anxiety, fear, guilt, shame, etc.) caused by intrusive thoughts (Abbott et al., 2017; See et al., 2022).

ER difficulties in OCD can cause an obsessive shift of attention to emotional stimuli, especially negative ones. Moreover, patients with OCD exhibit deficits in extinction of conditioning to aversive stimuli (Milad et al., 2013), which may indicate that attentional bias to stimuli with negative emotional valence is a major factor influencing impairment of inhibitory control. Existing studies indicate significant differences in eye movements in patients with OCD depending on the emotional valence of visual stimuli compared to healthy volunteers (Basel et al., 2023; Bradley et al., 2016).

In addition to the above, a shift of attention to negative stimuli and “getting stuck” on them in patients with OCD can lead to psycho-emotional exhaustion and a decrease in the level of adaptation to the environment. Adaptation of the functioning of the body to environmental changes is one of the main functions of the autonomic nervous system (ANS). People with affective and anxiety disorders exhibit dysfunctional regulation of the ANS. In patients with OCD, changes in ANS responses have been studied in less detail. Published studies show conflicting results, ranging from significant increases in heart rate (HR) to no differences between OCD patients and healthy volunteers either at rest or in response to aversive stimuli (for review, see Abbott et al., 2017). Psycho-emotional stress is often accompanied by an increase in the sympathetic tone of the ANS (Safonova & Shalamova, 2013). The temporal dynamics of the activity of the sympathetic and parasympathetic parts of the ANS under long-term stress reflects the ability to successfully cope with changing environmental conditions (Van Den Berg et al., 2015a).

Thus, studies of ANS reactions can play a decisive role in understanding the adaptive features of the ANS under cognitive-emotional load, and the study of oculomotor reactions using antisaccade task with stimuli of different emotional valence will help to understand the influence of emotional load on executive functions (inhibitory control and attention) in OCD.

1.2. Hypotheses, goals and objectives of the study

Hypotheses:

1. When performing the antisaccade task testing the integrity of inhibitory control, parameters of eye movements in the form of the number of errors and latency were increased in the OCD group compared to the control group;
2. Emotionally charged images of the negative spectrum have a more negative effect on the success of the antisaccade task compared to the control group;
3. Under conditions of cognitive-emotional load associated with performing the antisaccade task, the dynamics of ANS tone ((HR) and pupil area (PA)) in the OCD group are more maladaptive compared to the control group.

Research goals:

1. Identify oculomotor patterns that reflect the characteristics of executive functions in OCD (inhibitory control and attention), and the influence of emotional load on them;
2. To study the features of the dynamics of HR and changes of PA, reflecting the general adaptation of the ANS to the cognitive-emotional load in OCD.

Objectives:

1. Determining the scenario of the antisaccade task using stimuli of different emotional valence, providing a greater number of errors;
2. Analysis of oculomotor reactions, reflecting the functions of inhibitory control and attention, and the influence of emotional load on them, in patients with OCD and healthy volunteers using the antisaccade task;

3. Analysis of the dynamics of ANS tone based on changes in HR and PA during the performance of the antisaccade task in patients with OCD and healthy volunteers.

1.3. Theoretical and methodological justification

1.3.1. Theoretical background

The main neurobiological model of impaired inhibitory control in OCD involves an aberrant cortico-striatal-thalamo-cortical circuit (CSTC) (Karpinski et al., 2017; Norman et al., 2019; Saxena et al., 1998). The model of CSTC connectivity disruptions in OCD is based on an imbalance between excitatory glutamatergic and inhibitory GABA-ergic systems, as well as imbalances in serotonin and dopamine release (Brooks & Stein, 2015; Saxena et al., 1998).

The aberrant model of CSTC explains oculomotor control deficits in OCD (Jaafari et al., 2011; Kennard, 2011; Kloft et al., 2013). Oculomotor reactions reflecting executive functions are studied using various methods, including using antisaccade task (see review: Khayrullina et al., 2022). Impaired inhibitory control, reflected by increased errors in antisaccade task, is associated with altered anterior cingulate activity in OCD (Agam et al., 2010; Funch Uhre et al., 2022).

The first evidence for an OCD endophenotype came from a study by Lennertz et al., which found that patients with OCD and their healthy first-degree relatives exhibited increased error rates and increased response latencies on antisaccade task compared with healthy controls (Lennertz et al., 2012). Subsequently, Bey et al. confirmed this fact in a fairly large sample of 169 patients with OCD, revealing increased antisaccade latency, greater individual variability in antisaccade latency, and increased errors in antisaccade task in patients compared to the control subclinical group. A significant intergroup difference was manifested in errors in performing express saccades, while the OCD group did not significantly differ from the control group in errors in regular saccades. Trials with erroneous antisaccades were divided into express errors (latency from 90 to 140 ms) and regular errors (latency more than 140 ms).

Healthy relatives of patients with OCD also showed increased error rates and increased latency variability in antisaccade tasks. In first-degree relatives of patients with OCD, a positive correlation was observed between trait anxiety and the frequency of antisaccade errors, which may be explained by manifestations of a common endophenotype (Bey et al., 2018). Thus, most results from oculographic studies during antisaccade task indicate an impairment of inhibitory control in patients with OCD, manifested by increased latency (Maruff et al., 1999; Van Der Wee et al., 2006) and error rate (Agam et al., 2014; Narayanaswamy et al., 2021), which may be due to an imbalance in the transmission of excitation and inhibition in the CSTC circuit.

Studies of OCD involving the presentation of emotional stimuli have revealed structural changes and changes in functional activity in limbic regions (including the amygdala), parietal and occipital cortices, and the cerebellum (Hazari et al., 2019). Moreover, in OCD, linguistic stimuli of negative valence have been shown to influence inhibitory control and may cause impairment (Bannon et al., 2008; Bohne et al., 2005; Zetsche et al., 2015).

Existing studies support the influence of emotional stimuli on oculomotor responses in patients with OCD (Armstrong et al., 2010, 2012; Basel et al., 2023; Bradley et al., 2016). In a study by Bannon et al. participants with OCD demonstrated impairments in inhibitory control in response to negatively-valenced words in a «Facilitation/Inhibition task». The OCD group demonstrated increased levels of facilitation and lower levels of inhibition. However, this study did not use positive stimuli to determine differences in responses across all valences (Bannon et al., 2008). In any case, the impairment of inhibitory control in affective states can be explained using the concept that the expression of negative emotions is associated with rigidity in information processing, the basis of which lies in the person's excessive anxiety and his reaction to perceived danger (Beck et al., 1985; Williams et al., 1997). Patients with OCD have rigid “catastrophizing” beliefs about the consequences of their thoughts, which lead to high levels of anxiety, distress, guilt and shame (Rachman S. & Hodgson R., 1980). Impaired inhibitory control in people

with OCD also manifests itself under conditions of negative motivation, and specifically, patients with OCD demonstrated decreased response control under conditions of punishment, which manifested in an impulsive response style that was associated with their current severity of symptoms (Morein-Zamir et al., 2013).

Among other things, when studying oculomotor responses in patients with OCD, Armstrong et al. found increased attention and difficulty shifting attention when viewing images of fearful faces during free viewing and visual search tasks (Armstrong et al., 2012). Moreover, volunteers with high levels of fear of contamination paid more attention to faces with expressions of fear and disgust than the group with low levels (Armstrong et al., 2010). Also, the severity of OCD symptoms was positively correlated with the frequency and total duration of fixation on OCD-relevant stimuli (e.g., images of dirt), possibly reflecting a shift in attentional focus to negative images and/or stimuli associated with a specific type of OCD (Bradley et al., 2016).

Based on an analysis of gaze fixation parameters, Bradley et al. proposed the «vigilance» and «maintenance/delayed disengagement» model as a likely cause of attentional bias (Bradley et al., 2016). The «vigilance» hypothesis suggests that OCD patients attend to OCD-related stimuli more quickly than controls, and the «maintenance/delayed disengagement» hypothesis suggests that OCD patients tend to fixate on negative stimuli for longer periods of time and cannot switch to other stimuli. OCD symptom severity was indicated by greater frequency and overall duration of gaze fixations on OCD-relevant stimuli, possibly reflecting an attentional bias (Bradley et al., 2016). Longer fixation on negative stimuli (Toffolo et al., 2016) may also support the «maintenance/delayed disengagement» hypothesis. Basel et al., 2023 suggest that findings supporting the «vigilance» and «maintenance/delayed disengagement» hypotheses in OCD are task dependent (Basel et al., 2023). Previous studies have used different experimental designs, which may lead to mixed interpretations.

Increased anxiety, characteristic of patients with OCD, can lead to maladaptation in changing environmental conditions. The body's adaptation to

environmental changes depends on the functioning of the ANS. Very important in this case is the balanced interaction of the sympathetic and parasympathetic tone of the ANS. Evidence suggests that individuals with decreased parasympathetic control during periods of stress coupled with increased vagal control during rest demonstrate more adaptive social and emotional functioning (Gramzow et al., 2008). The temporal dynamics of the activity of the sympathetic and parasympathetic parts of the ANS under long-term stress reflects the ability to successfully cope with environmental conditions (Van Den Berg et al., 2015b). Longer periods of predominant parasympathetic tone correlate with more adaptive ER strategies and reduced risk of cardiovascular disease (Buccelletti et al., 2009; Porges, 2007; Thayer et al., 2012). Psycho-emotional exhaustion can cause corresponding tension, often accompanied by an increase in sympathetic tone (Safonova & Shalamova, 2013).

The pathogenesis of many mental illnesses is associated with weakening of adaptation mechanisms and dysregulation of the ANS. In particular, ANS dysfunction may be observed in schizophrenia, characterized by increased sympathetic and decreased parasympathetic activity, resulting in increased HR, altered pupillary response, and increased salivation or sweating (Stogios et al., 2021). Some researchers suggest that schizophrenia may result from a combination of two factors: ANS dysfunction and an environmental immune trigger (Carnac, 2022). In addition, it has been shown that emotional stress in individuals with affective and anxiety disorders is accompanied by dysregulation of the ANS with a predominance of sympathetic tone. Individuals with increased social anxiety had poorer HR regulation and lower heart rate variability. Weak modulation of vagal tone was associated with greater social anxiety, and lower vagal tone was associated with greater defensive mechanisms and less sensitivity to behavioral activation (Abbott et al., 2017). Previous studies have shown that patients with post-traumatic stress disorder (PTSD) exhibit higher HR reactivity in response to unpleasant affective stimuli. Higher resting HR and higher HR activity when mentioning trauma in people with PTSD have been explained as excessive ANS activation. Pupillometric studies have shown that, compared with healthy volunteers, PA in

patients with depression was significantly greater in both darkness and at the point of minimum pupil constriction (Wang & Munoz, 2014). Moreover, in major depressive disorder and seasonal affective disorder, atypical pupil dilation may be an indicator of deterioration in the patient's condition (Roecklein et al., 2013).

Research on ANS responses in OCD is limited. Published studies show conflicting results, ranging from a significant increase in HR in OCD to no difference between the OCD group and healthy controls at rest and during emotional load (Abbott et al., 2017). Olbrich et al. provide evidence of increased sympathetic tone in patients with OCD (Olbrich et al. 2022), and Herzog & Brakoulias describe an association between decreased heart rate variability and OCD symptom severity (Herzog & Brakoulias 2022). Thus, further research into HR regulation may play a critical role in understanding the characteristics of emotion dysregulation in individuals with OCD.

Studies of pupillary response in OCD also have heterogeneous results under different experimental conditions (Gürsel et al., 2018; Leuchs et al., 2019). Pupillary response was studied during fear conditioning and extinction tasks. In particular, patients with OCD showed greater PA during psycho-emotional load (Pöhlchen et al., 2021). However, there is practically no data on changes in mental health in patients with OCD when viewing emotional images of different valence under conditions of cognitive load.

1.3.2. Research methodology

The antisaccade task is a reliable and sensitive tool in psychopathology, particularly in OCD, since the degree of success in the antisaccade task depends on the complete functioning of fronto-subcortical brain regions (Hutton & Ettinger, 2006; Narayanaswamy et al., 2021). In the antisaccade task, participants must consciously suppress a reflexive eye movement (prosaccade) to focus gaze on a visual peripheral stimulus and instead perform a goal-directed eye movement to the opposite point in the visual field (antisaccade). An error in this task is considered to be a failure to suppress a reflexive prosaccade to a stimulus. Performance of the

antisaccade task recruits fronto-parietal regions, primarily the frontal eye field (FEF), supplementary eye field (SEF), dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex, posterior parietal cortex, thalamus, and striatum (Hutton & Ettinger, 2006).

Since the antisaccade task has been shown to be effective in assessing executive functions in OCD (Bey et al., 2016), this, in turn, influenced our choice of research methodology using a modification of the antisaccade task in which images of different emotional valence served as fixation stimuli.

There are various scenarios for antisaccade tasks, but the main ones are the «step», «gap» and «overlap» scenarios, which differ in the chronology of presentation of fixation and target stimuli. These scenarios differ in the time intervals between the end of the presentation of the central fixation image and the appearance of the target stimulus. In the «step» scenario, the target stimulus is presented immediately after the end of the fixation stimulus on one side of the screen. The «gap» scenario is characterized by the disappearance of the fixation stimulus and its absence on the screen for 200 ms, after which the target stimulus is presented on one side of the screen. In the «overlap» scenario, the fixation stimulus lasts for 200 ms. lingers on the screen along with the target one, and after the fixation stimulus disappears, the participant needs to make antisaccade. Taylor & Hutton indicated that the performance of antisaccade task depends on the nature of the instruction, and also demonstrated that the number of antisaccade errors and latencies can vary significantly depending on the modification of the antisaccade task (Taylor & Hutton, 2009). Each antisaccade task design showed different oculomotor response patterns in a sample of volunteers with attention deficit hyperactivity disorder (ADHD) (Goto et al., 2010; Munoz et al., 2003; Siqueiros Sanchez et al., 2020). Before experimental studies involving the OCD group, our goal was to test different scenarios of the antisaccade task («step», «overlap», «gap») on highly anxious young volunteers with different levels of impulsivity, without established mental pathologies. The selection of this category of participants was based on the fact that high levels of impulsivity and anxiety are key premorbid features of mental disorders

such as ADHD, substance abuse, OCD and other mental disorders (Nigg, 2013; Summerfeldt et al., 2004).

1.4. Scientific novelty

1.4.1. Theoretical novelty

Most results from studies of eye movements during antisaccade task point to impaired inhibitory control in patients with OCD. At the same time, images of neutral valence, such as geometric shapes, were usually used as stimuli (Bey et al., 2018; Narayanaswamy et al., 2021), and therefore it was impossible to determine the influence of cognitive-emotional load on executive functions that control goal-directed eye movements.

A feature of OCD is increased anxiety, and the manifestation of compulsions is a maladaptive strategy for ER. Therefore, the use of emotional stimuli in the antisaccade task is important for understanding the influence of emotionally charged environmental changes on executive functions. In this regard, in Study 1, in the antisaccade task, in addition to neutral stimuli, we also used emotional stimuli (positive, negative). Also, taking into account the fact that the antisaccade task has different types of scenarios («step», «overlap», «gap»), we studied their influence with stimuli of different emotional valence on oculomotor reactions to determine the optimal strategy for solving the antisaccade task. The study was conducted on healthy young volunteers with high levels of anxiety and different levels of impulsivity.

Having determined the optimal scenario for antisaccade task with stimuli of different emotional valence (neutral, positive, negative) in the form of an «overlap» scenario, in the 2-nd study we applied it to the OCD group and the control group, examining their oculomotor reactions, which reflect both executive functions and the influence of emotional load on them.

Among other things, given that adaptation to changing environmental conditions depends on the full functioning of the ANS, we also examined the influence of cognitive-emotional load on it through the prism of studying the dynamics of HR and PA in study 3.

1.4.2. Methodological novelty

We first applied the antisaccade task with different temporal scenarios («step», «overlap» and «gap») using images of different emotional valence as fixation stimuli.

Also, the antisaccade task «overlap» scenario with stimuli of different emotional valence was used for the first time for a comprehensive study of the psychophysiological characteristics of executive functions and the influence of emotional stimuli on them through the prism of oculomotor and autonomic reactions.

1.5. Theoretical and practical significance

The theoretical significance of the obtained research results is determined by the fact that they are important for a comprehensive understanding of the psychophysiological characteristics of executive functions in OCD and their connection with ER. We have shown that patients with OCD do not have impaired inhibitory control in general, and its deterioration occurs when stimulated by negatively colored stimuli, which is apparently accompanied by a shift of attention to them. Maladaptation to environmental changes in patients with OCD is manifested by increased sympathetic tone and more rigid dynamics of the ANS in the form of reduced adaptation of the ANS to cognitive-emotional load. Thus, the theoretical significance of our work lies in the fact that the results of our studies show a deterioration in executive functions due to emotional dysregulation and general maladaptation of the psyche to environmental changes.

The practical significance of the study is that the antisaccade task can be used for the early diagnosis of OCD, and also be an intermediate diagnostic tool for studying executive functions after treatment with selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioral therapy. Also, using the antisaccade task using stimuli of different emotional valence, in the future it is possible to comprehensively study executive functions and their relationship with emotional perception in patients with ADHD, who are characterized by impaired inhibitory control, as well as borderline personality disorder (BPD), characterized by emotional

dysregulation, which in the future, it may help to distinguish the psychophysiological characteristics of executive functions in these disorders (OCD, ADHD and BPD) based on data from oculomotor and autonomic reactions.

1.6. Provisions for the defense

1. The scenario of the antisaccade task with overlapping time of display of target and fixation stimuli of different emotional valence (neutral, positive, negative) can be used for an objective study of the influence of impulsivity on executive functions under cognitive-emotional load;

2. Decreased inhibitory control of goal-directed eye movements during the perception of emotionally negative images reflects the influence of emotional dysregulation on executive functions in OCD;

3. Cognitive-emotional load causes a greater increase in the sympathetic tone of the ANS in patients with OCD than in volunteers from the subclinical group;

4. In OCD, the level of adaptation of the ANS to cognitive-emotional load is reduced, accompanied by a decrease in inhibitory control in response to negative stimuli.

1.7. Author Contribution

Study 1: Study concept and design, data collection, data analysis and interpretation, data visualization, article writing.

Study 2: Study concept and design, data collection, data analysis and interpretation, data visualization, article writing.

Study 3: Study concept and design, data collection, data interpretation, article writing.

2. DESCRIPTION OF THE STUDIES

In this chapter we describe the main points of the research methodology, design, results and main conclusions. In the first part, we described a methodological study aimed at determining the optimal design of antisaccade task using stimuli of different valence. In the second part, we described an experimental study of oculomotor reactions reflecting the psychophysiology of executive functions and their relationship with emotional perception, using the antisaccade task «overlap» design (as the most optimal) with stimuli of different valence relative to the OCD group and the control group. In Part 3, we described an experimental study of autonomic reactions and their dynamics under cognitive-emotional load in terms of HR and PA parameters in the OCD group and the control group.

2.1. Study I. Features of oculomotor reactions in highly anxious volunteers with different level of impulsivity in solving different types of the antisaccade task

To determine the optimal time scenario for the antisaccade task, we conducted a methodological study on clinically healthy but highly anxious volunteers with different levels of impulsivity using different scenarios for the antisaccade task («step», «overlap», «gap»). The selection of this category of participants was based on the fact that high levels of impulsivity and anxiety are key premorbid features of mental disorders such as OCD, ADHD, substance abuse and other personality disorders (Nigg, 2013; Summerfeldt et al., 2004).

Our goal in this study was to apply the main types of experimental scenarios of the antisaccade task («step», «overlap», «gap») using fixation stimuli of different emotional valence and compare the results depending on the specifics of the antisaccade task.

Participants

Thirty-four highly anxious volunteers (26 women, 8 men), including 20 low-impulsivity volunteers (59.7 ± 7.4) and 14 higher-impulsivity volunteers (74.9 ± 4.5), were recruited to participate in a psychological study. The level of anxiety was

determined based on participants' completion of the Russian version of the State Trait Anxiety Inventory (STAI), the level of impulsivity was determined based on the Barratt scale (BIS-11). The level of anxiety did not differ between the groups: in low-impulsive volunteers - 51.3 ± 4.8 , in high-impulsive volunteers - 50.9 ± 10.1 . The average age of the volunteers was 20.2 ± 0.6 years. All participants were right-handed, and the dominant eye was determined using the Dolman method (Cheng et al., 2004). Exclusion criteria included the following grounds: (a) history of substance abuse; (b) mental or neurological disorders; (c) uncorrected vision.

Study procedure and stimuli

The paradigm consisted of three blocks of antisaccade tasks with different time intervals between the end of the presentation of the central fixation image and the appearance of the target stimulus: block 1 – «step»; block 2 – «overlap»; block 3 – «gap». Each participant completed a total of 300 antisaccade tasks. Each block consisted of 100 trials, in which 60 fixation stimuli were images of neutral emotional valence, 20 trials of positive valence, and 20 trials of negative valence. To prevent the habituation effect and consolidate the surprise effect, there were more neutral stimuli. Positive and negative images were taken from the International Affective Picture System (IAPS) (Lang et al., 2008) and varied in mean valence and mean arousal ratings. The average valence of positive stimuli was 7.4 ± 0.4 , the average arousal was 4.9 ± 0.7 . The average valence of negative stimuli is 2.2 ± 0.5 , the average arousal is 6.1 ± 0.7 . All blocks had a different set of negative and positive images. Positive images included images of a «family», «smiling children», «landscapes», «animals» and «dishes». Negative images included «mutilation», scenes of «assault» and «violence», «disaster» and «pollution» (Lang et al., 2008; Mikels et al., 2005). Of the 120 emotionally charged images (positive, negative) we used, 9 images had minor differences relative to the Russian sample. 5 positive images («family», «mountains», «child», «seals», «cupcake») rated by the Russian sample had greater arousal than the American sample ($+1.64$); no cross-cultural differences were found in valence. 1 negative image («hospital») in the Russian

sample had a more significant negative valence (+0.7) and greater arousal (+0.6). Images in the form of mutilation had a greater negative valence (+0.2), «eye disease» and «burial» had a greater arousal (+1.1) in the Russian sample (Vasanov et al., 2011). In general, in a study conducted on a Russian sample, when presented with images similar to those from the IAPS, almost identical results were obtained in both valence and arousal to the IAPS results (Vasanov et al., 2013). The neutral stimulus was a circle, which did not change in all presentation blocks. After the participant completed each trial of the antisaccade task, a black screen appeared for a duration of 1000 ms (break between trials) in all blocks of the antisaccade task (Fig. 1).

Each task began with the presentation of a central fixation stimulus, which remained on the screen for 700–1500 ms. There were 2 small squares on either side of the central fixation stimulus. When performing 1 block («step» scenario), after the disappearance of the fixation stimulus, the target stimulus appeared in two possible horizontal locations, $\pm 6^\circ$ of visual angle from the center. The target stimulus was the same image as the central fixation stimulus, lasting 1000 ms. The task in the «step» scenario was to look in the mirror direction of the image.

In the scenario of the antisaccade task of the «overlap» type (with the time of presentation of fixation and target stimuli overlapping), the target stimulus was one of two small squares standing on either side of the central fixation stimulus. After an interval of 700–1500 ms, as in the «step» design, only the fixation stimulus with one square on one side remained on the screen, and the second square disappeared. After 200 ms, the central fixation stimulus disappeared, and the square remained on one side of the screen. The target stimulus (square) was on the screen for 800 ms in two possible locations, $\pm 6^\circ$ of visual angle from the center. The challenge in the «overlap» design was to look in a mirror direction from the remaining square on the screen.

In the «gap» scenario, the central fixation stimulus, as in other variations of the antisaccade task, remained on the screen for 700 - 1500 ms. After it expired within 200 ms, only 2 squares remained on the right and left sides of the center. After a pause of 200 ms, the target stimulus appeared on one side. The target stimulus was

the same image as the central fixation stimulus and lasted 800 ms. The target stimulus appeared either left or right of center at $\pm 6^\circ$ of visual angle from center. The task in the «gap» design was to look in the mirror direction of the target stimulus on the screen.

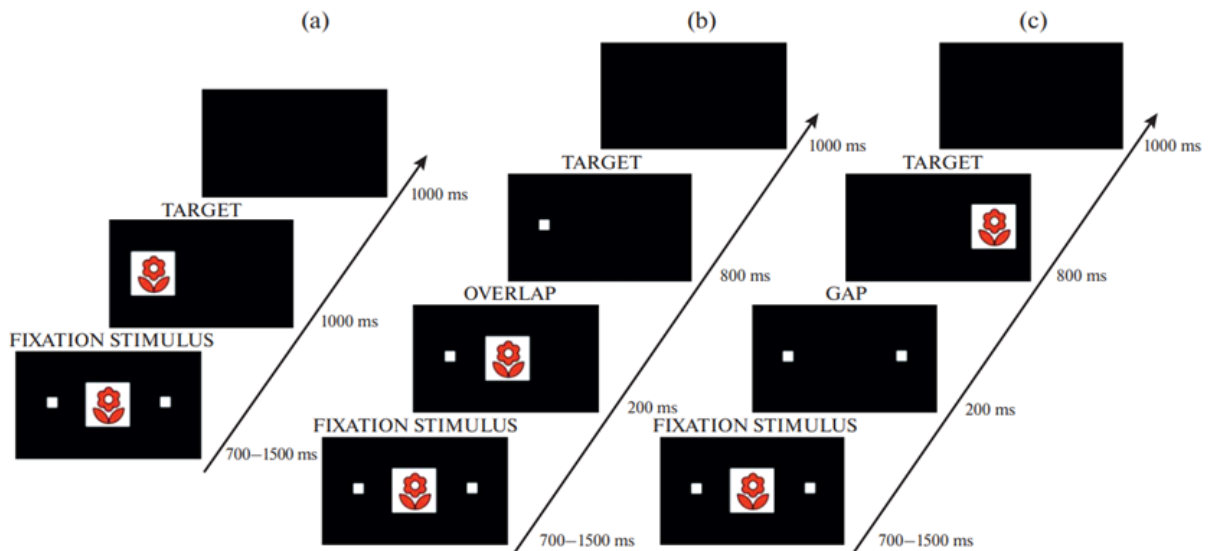


Figure 1. The study paradigm with stimuli: (a) «step» design, (b) «overlap» design, (c) «gap» design. The flower picture is a substitute of image taken from IAPS.

Data analysis

Data preprocessing was carried out using Data Viewer software (SR Research, Canada). Trials with artifacts (blinking, etc.) were excluded from the analysis. Further analysis was carried out in RStudio (<https://www.rstudio.com/>). The data were divided into trials with correct antisaccades and trials with incorrect antisaccades. Trials with erroneous antisaccades were divided into express errors (latency from 90 to 140 ms) and regular errors (latency more than 140 ms).

For each stimulus valence within three types of the antisaccade task scenarios, the following parameters were measured for all participants in both groups: frequency of regular antisaccade errors, frequency of express antisaccade errors, average latency time of correct antisaccades, average latency time for express and regular antisaccade errors, average amplitude correct antisaccades, average amplitude for express and regular antisaccade errors, average velocity for correct antisaccades, average velocity for express and regular antisaccade errors.

Statistical analysis

Statistical analysis of oculomotor reaction indicators was carried out in both groups for each parameter for each emotional valence within three types of design antisaccade task (R-Studio). With a normal distribution, the studied parameters were compared using analysis of variance (ANOVA). The ANOVA used 2 levels of comparison between groups (participants with LI & HA and HI & HA), 3 levels of blocks («step», «overlap», «gap») and 3 levels of stimulus valence (neutral, positive and negative). If the ANOVA showed a significant effect, a pairwise comparison (Tukey's HSD test) was used as a post hoc comparison. In case of non-normal distribution, the Kruskal-Wallis test was used as a nonparametric equivalent of analysis of variance and Dunn's test as a post hoc test, respectively.

Results

In the «step» block, the studied eye movement patterns did not differ either in the valence of the stimuli or between the groups. In the «overlap» block, only the regular error mean latency differed significantly between groups on trials with neutral stimuli [$H(1, 34) = 5.33, p < 0.05$]. The regular error mean latency was significantly higher in individuals with high impulsivity compared to participants with low impulsivity ($p = 0.0105$ by Dunn's test) (Fig. 2 (a)). This result is partly consistent with studies showing that participants with ADHD and OCD with high levels of impulsivity performed the antisaccade task with increased antisaccade latency compared to controls (Goto et al., 2010; Hakvoort Schwerdtfeger et al., 2013; Hu et al., 2013 al., 2020; Sekaninová et al., 2019). The increase in antisaccade latency reflects the additional processing time required to suppress the reflexive saccade toward the peripheral stimulus and modify the saccade program to produce antisaccade (Maruff et al., 1999). An imbalance between voluntary and automated saccadic impulses results in regular latency direction errors (Coe & Munoz, 2017). Since participants in both groups showed increased trait anxiety, it can be assumed that the observed differences in the latency of regular errors reflect precisely the combination of increased anxiety and increased impulsivity. In the antisaccade task,

the thoughtless desire to solve the problem as quickly as possible, characteristic of impulsive behavior (Levine et al., 2007), is expressed in reducing attention to the fixation stimulus and immediately following it with the gaze in the direction of the target stimulus or in the opposite direction from it. Therefore, highly impulsive people find it easier to shift attention in rapidly changing conditions, for example, in «step» and «gap» blocks. The «overlap» design allows participants to know the target stimuli in advance, but the response must be given later. Waiting for the right moment to respond slows down the shift of attention, increasing the time it takes to make a decision, especially in the absence of an emotional context. The low semantic content of neutral stimuli can lead to a decrease in concentration of attention, which is associated with long latency of regular errors in highly impulsive participants.

In the «gap» block, the regular error mean amplitude saccades differed significantly between groups [$H(1, 31) = 3.63, p < 0.05$] in response to neutral stimuli. The regular error mean amplitude was significantly greater in the low-impulsivity group compared to the high-impulsivity group ($p = 0.033$ by Dunn's test (Figure 2(b))). The decrease in the regular error mean amplitude in the «gap» design may also reflect high-impulsivity behavior. In the «gap» task, when events on the screen changed (appearance and disappearance of the target stimulus), highly impulsive participants, even after making an error, could quickly turn on and redirect the saccade in the desired direction, which may indicate a high level of impulsivity. Impulsivity does not always have a negative impact on performance. tasks. Decision making with impulsivity may not only be ineffective, as indicated in most studies, but also highly effective in both the speed and quality of problem solving. In future studies, we would propose to classify impulsive people based on primary neuropsychological tests.

Comparison of blocks in both groups showed that eye movements in the «overlap» block differed from the «step» and «gap» blocks. The amplitude, velocity and latency of correct antisaccades in the «overlap» block were significantly lower than in other types of temporal task scenarios ($p < 0.001$ by Dunn's test). In contrast,

express and regular error rates, the express error mean amplitude, the regular error mean amplitude, latency and velocity were higher than in the other blocks ($p < 0.001$). Moreover, values of express error mean latency ($0.001 < p < 0.01$) and express error mean velocity ($0.001 < p < 0.05$) were the largest for «overlap» block and the lowest for «step» block.

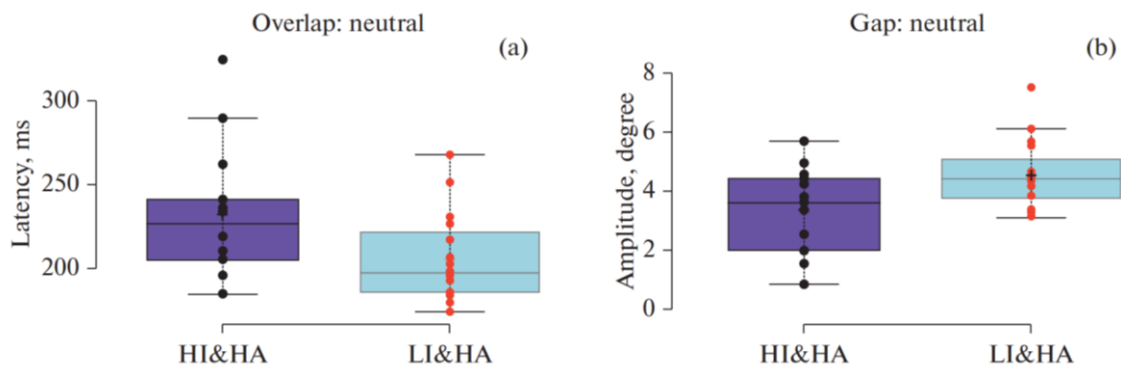


Figure 2. Between-group comparison of saccade parameters in the trials with neutral stimuli: (a) mean latency for regular error saccades in the «overlap» design, (b) mean amplitude for regular error saccades in the «gap» design. HI&HA – high impulsivity and high anxiety group, LI&HA – low impulsivity and high anxiety group.

Conclusions

The findings indicate variability in antisaccade errors in both groups without any intergroup and intragroup dependence on the design or emotional valence of the stimuli. The percentage of express errors was within the population range ($< 25\%$) in all blocks for all groups (Maruff et al., 1999). The percentage of regular errors was also within the population range in the «step» and «gap» blocks for both groups, whereas the percentage of antisaccade errors in the «overlap» block was above population values in both groups. In studies (Blekic et al., 2021; Liang, 2018), participants with high anxiety performed antisaccade tasks and demonstrated correct antisaccades with longer latencies compared to controls, while the number of directional errors depended on the design of the paradigm. Our study partially replicates these results, as we showed that the error rate exceeds 25% only in the «overlap» block. Based on the results of this study, we chose the «overlap» scenario of the antisaccade task for further study of executive functions (inhibitory control and attention) and the influence of cognitive-emotional load on them in patients with OCD.

2.2. Study II. Increased error rate and delayed response to negative emotional stimuli in antisaccade task in OCD

Having tested and determined the optimal design of the antisaccade task in the form of an “overlap” design (Part 1), we conducted an experimental study of the influence of stimuli of different valence on executive functions when performing the antisaccade task in the OCD group and the control group. Based on the presence of high anxiety in patients with OCD, we hypothesized that emotional stimuli may worsen the quality of performance of the antisaccade task in the group with OCD.

Participants

Thirty-two patients with OCD (24.5 ± 6.17 years, 21 women) and thirty control volunteers (22.5 ± 5.15 years, 17 women) took part in the study. A structured interview was conducted with all participants by a clinical psychologist. To determine the severity of OCD, volunteers also completed the Y-BOCS test. 23 patients in the OCD group received drug therapy, and the remaining 9 participants did not have drug therapy. To check the possible influence of medication on the studied parameters, we conducted a regression analysis of each of the studied parameters of oculomotor reactions, taking into account the therapy. In the regression analysis, the state of the pharmacotherapy used was considered as a covariate factor (1 – yes, 0 – no). Additionally, the type of drugs used was analyzed (0 - none, 1 - antidepressants (14 patients), 2 mood stabilizers (9 patients)). No effect of medication was found.

In addition, previous studies of oculomotor responses to medications (benzodiazepines, first- and second-generation antipsychotics, antidepressants) have found no effect of these medications other than a decrease in peak saccade velocity (Crawford et al., 1995; Green & King, 1998; Lynch et al., 1997; Reilly et al., 2008).

At the time of participation in the study, all patients were in a stable phase of the disorder. Drug abusers and those with neurological and mental disorders other than OCD (bipolar disorder, autism spectrum disorder, schizophrenia) were excluded from the group.

Study procedure and stimuli

The antisaccade «overlap» design paradigm consisted of 3 blocks of antisaccade tasks. In total, each participant completed 300 antisaccade tasks across all three blocks. Each block contained 100 trials, of which 60 trials contained images with neutral valence, 20 trials - positive and 20 trials - negative valence as fixation stimuli. To prevent the habituation effect and consolidate the surprise effect, there were more neutral stimuli. Positive and negative images were taken from the International Affective Image System (Lang et al., 2008) and differed in mean valence and mean arousal. All blocks had a different set of negative and positive images. The neutral stimulus was a circle, which did not change in all presentation blocks. The stimuli for each trial appeared on a screen with a black background. Fixation stimuli were images (neutral, positive, negative) in the form of squares 250*300 mm, and target stimuli were small squares 14*14 mm, located on both sides of the fixation point. The target stimuli were located on the left and right sides of the center of the fixation image (Fig. 3). A detailed description of the antisaccade task «overlap» design is described in Study 1.

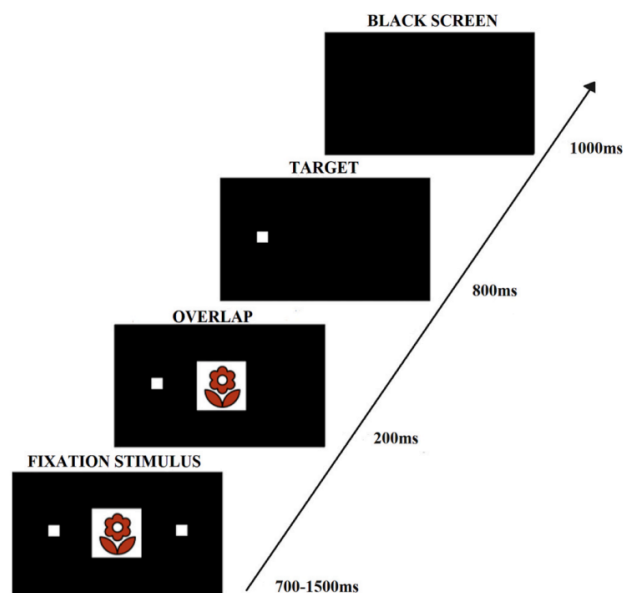


Figure 3. The «overlap» design of antisaccade task paradigm with a substitute of the stimulus.

Data analysis

Data preprocessing was conducted using Data Viewer (SR Research). Trials with artifacts (blinks, etc.) and trials with a latency of less than 80 ms were excluded from the analysis. Further analysis was performed in R Studio

(<https://www.rstudio.com/>). For all participants in both groups, the following parameters were measured for each stimulus valence: error rate; average latency of correct antisaccades; average velocity of correct antisaccades.

Statistical analysis

Statistical analysis of the parameters of oculomotor reactions was carried out in both groups for each stimulus valence. The mixed model ANOVA used 2 levels of between-group comparisons (participants with OCD and controls) and 3 levels of within-group comparisons of valences (neutral, positive, negative). If the analysis of variance showed a significant effect, the Bonferroni post hoc method was used.

Results

The groups (control and OCD) did not differ significantly in age distribution (22.5 ± 5.2 vs. 24.5 ± 6.2 years; $p > 0.05$). Gender distribution was also similar between groups (X-square = 0.52019, $p = 0.4708$). The level of obsessive-compulsive symptoms (Y-BOCS - 20.9 ± 8.27 vs. 1.2 ± 2.06 , $p > 0.05$) differed significantly between the OCD and control groups. The error rate (Fig. 4) when performing antisaccades differed significantly between groups [$F(1, 60) = 4.64$, $p < 0.01$]. Post hoc analysis showed that patients with OCD had a higher error rate on trials with negative valence images than controls [$F(1, 60) = 7.17$, $p < 0.01$]. Statistical differences were also found in valence in both groups [$F(2, 120) = 12.78$, $p < 0.01$]. Statistical differences were found in the valence factor: both groups made more errors in tests with images of negative valence than neutral [$t(61) = 4.34$, $p < 0.01$] and positive [$t(61) = 3.05$, $p < 0.01$]. Moreover, the OCD group (an interaction term between group and valence within OCD group) showed statistical differences between valence conditions as it made more errors on negative-valence trials than on neutral-valence trials [$t(31) = 4.58$, $p < 0.01$] and positive [$t(31) = 3.44$, $p < 0.01$]. Within the control group, no statistical differences were found between valences in relation to error rates.

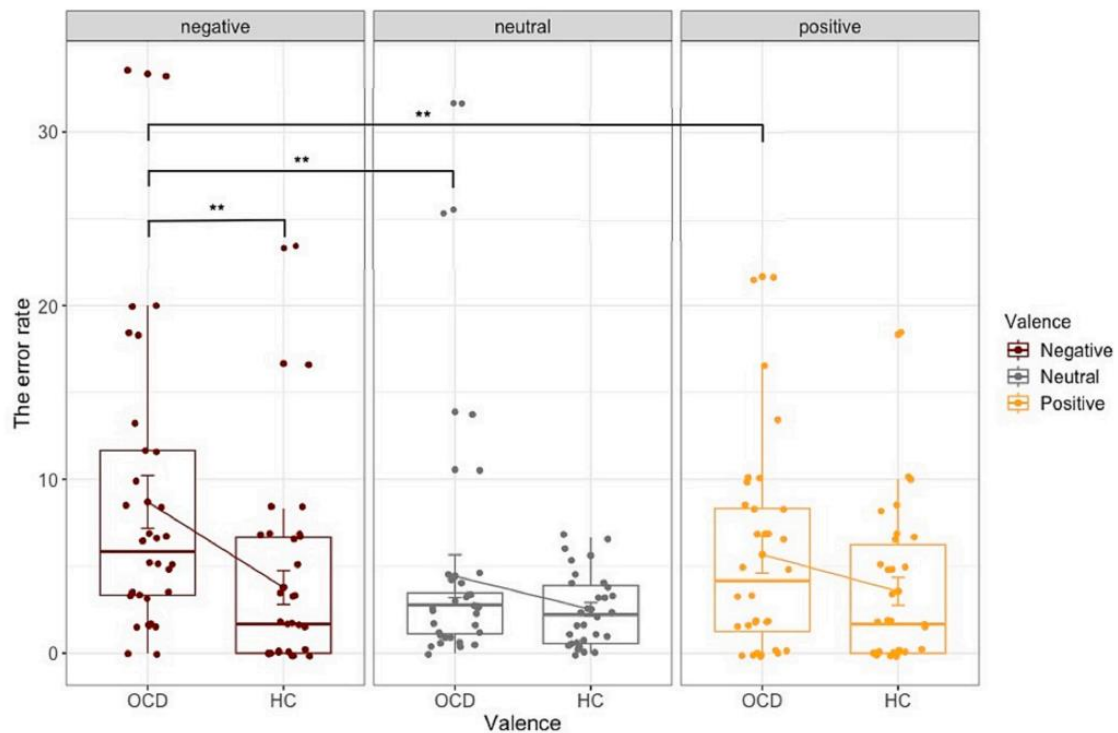


Figure 4. The error rate differences between groups (*HC - healthy control, OCD - obsessive-compulsive disorder)

The latency of correct antisaccades (Fig. 5) varied significantly as a function of valence in the OCD group [$F(2, 120) = 3.92, p < 0.01$]. Post hoc analyzes showed that latency was higher for negative valence than for positive valence [$t(31) = 4.3, p < 0.01$], and for neutral valence than positive valence [$t(31) = 2.91, p < 0.01$]. No statistical differences between valences were found within the control group. Statistical differences in both groups were found in the valence factor [$F(2, 120) = 5.22, p < 0.01$]. In both groups, latency was higher with negative valence than with positive valence [$t(61) = 3.12, p < 0.01$], longer with neutral than with positive valence [$t(61) = 2.6, p < 0.05$].

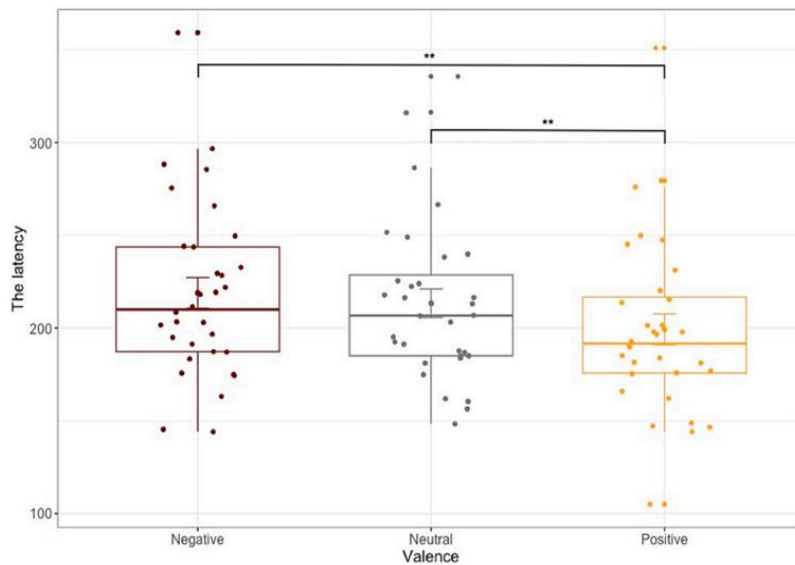


Figure 5. The correct antisaccade latency differences in OCD group.

The average velocity of correct antisaccades (Fig. 6) showed differences between valences in both groups [$F(2, 120) = 12.46, p < 0.01$]. The average velocity of correct antisaccades was higher for negative valence than for neutral [$t(61) = 4.43, p < 0.01$], and for neutral than with positive valence [$t(61) = 3.92, p < 0.01$] in both groups. However, the groups did not differ from each other.

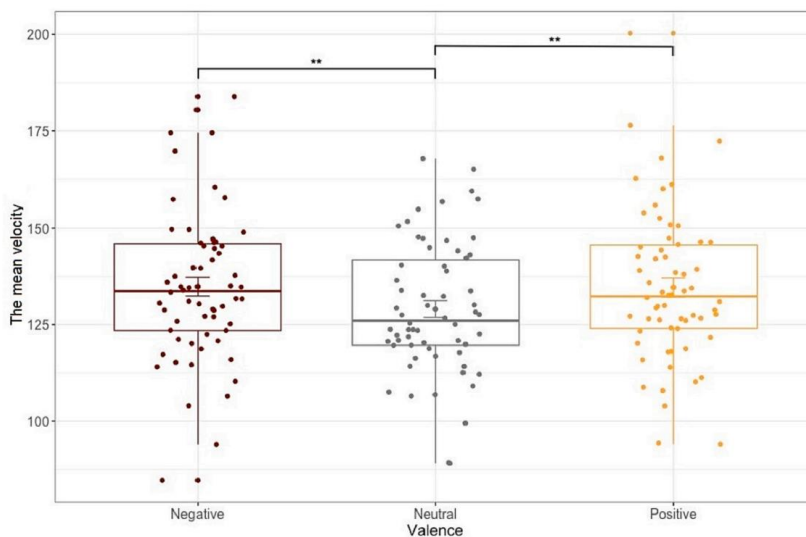


Figure 6. The correct antisaccade mean velocity differences between valences.

Conclusions

The modified antisaccade «overlap» design task we developed with images of different emotional valence (neutral, positive, negative) allows us to study executive

functions (inhibitory control and attention) and the influence of cognitive-emotional load on them. The OCD group made more antisaccade errors in trials when fixation stimuli had a negative emotional valence, which supports the hypothesis that negative stimuli influence inhibitory control in the development of OCD. The latency of a correct antisaccade in the OCD group to negative and neutral stimuli was significantly higher than to positive ones. This may indicate that negative stimuli for participants with OCD were significant, and therefore the latency of correct antisaccades naturally increased, since additional time was required to process them. It can be assumed that the increase in latency to neutral stimuli is due to the fact that neutral stimuli were monotonous and of the same type, and their number was generally greater. At the same time, it is impossible to draw a conclusion about an impairment of general inhibitory control in OCD based on our data, since there were no statistical differences in error rate within the control group in relation to neutral images. Both groups showed increased average velocity of antisaccades in response to negative and positive stimuli compared to neutral ones, confirming research findings that responses to emotionally charged stimuli occur faster and have a higher priority, which in general appears to be evolutionary-adaptive value (Pilarczyk & Kuniecki, 2014).

2.3. Study III. Dynamics of the autonomic nervous system during cognitive-emotional load in obsessive-compulsive disorder

In parallel with experimental study 2 on the influence of stimuli of different emotional valence on executive functions (inhibitory control and attention) when performing the antisaccade task «overlap» design in the OCD group and the control group, we examined the ANS reaction in the form of HR and PA, as well as the dynamics of ANS reactions during the antisaccade task. We tested the hypothesis that, under the influence of cognitive-emotional load, the OCD group would demonstrate more rigid ANS responses compared to the control group.

Participants

The analysis used data from a sample of participants whose demographics were described in Study 2. Data of ANS for one participant in the OCD group were not recorded for technical reasons, so subsequent analyzes were conducted on data from 31 participants in this group. Just like in the second study, a regression analysis was carried out for each of the studied parameters of HR and PA, taking into account the ongoing drug therapy. No influence of the drug intake factor on the studied ANS reactions was found.

Study procedure

The antisaccade task with an «overlap» design was described in Studies 1 and 2. As participants performed the antisaccade task, we recorded changes in PA in fixation period using an EyeLink Portable Duo eye-tracker. For HR monitoring, we used the auxiliary channels of the BrainVision actiCHamp Plus amplifier, the sensor was attached to the index finger of the right hand.

Data analysis

The trial report in EyeLink Data Viewer (Version 4.1.1) provided the pupil size mean parameter, which represents the average pupil size in arbitrary units for the trial. Data were exported for the fixation on stimuli period. Further preprocessing of the PA was carried out via Rstudio (version 2023.03.0+386). All data were analyzed at the onset of fixation stimuli in the order of their presentation in each block. HR recordings were preprocessed using MATLAB R20202b (Version 9.9.0.1467703). HR parameters were calculated for each RR distance (interval between two heartbeats) throughout the entire time period for each block.

To assess the dynamics of HR, we divided the entire duration of each experimental block into 50 units lasting at least 10 seconds. This division was based on previous studies that found that a 10-second ECG recording was sufficient to accurately estimate HR (Shuai, 2016). Next, all values were normalized using the Z-

transform (for each participant individually and the entire recorded fragment) (Fig. 7). Normalized data were used for further analysis of the dynamics of HR and PA.

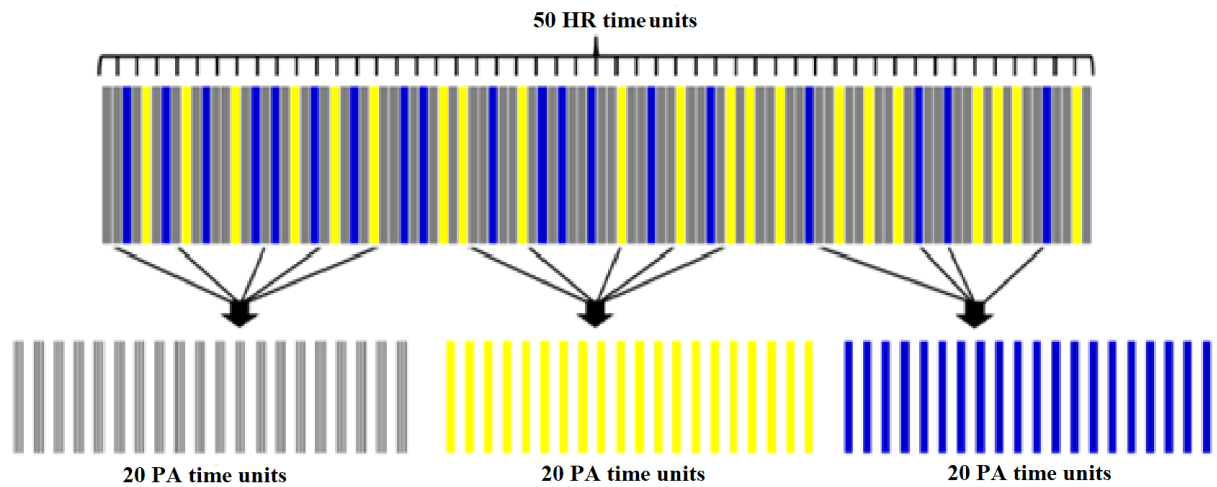


Figure 7. Scheme of the experimental design: temporal analysis of the heart rate (HR) – 50 units, and temporal analysis of the pupil area (PA) data – 20 units for negative, positive, and neutral stimuli.

We determined the latencies and amplitudes of the individual minimum and maximum points of the HR changes for each participant, as each block began with an elevated HR level that gradually decreased within the first two minutes, reaching its minimum point approximately one minute after the beginning, and then increased until the maximum point at about seven or eight minutes from the beginning.

Each PA value was analyzed according to the period of presentation of fixation stimuli for each experimental block (the first 700 ms). Neutral stimulus values were averaged across three consecutive stimuli. All values were calculated using the average of the entire recorded units for each participant. Trials with artifacts (blinking, etc.) were excluded from the analysis. Subsequently, the PA data was used to analyze the dynamics of the PA.

Statistical analysis

To compare the temporal dynamics between groups, taking into account all calculated units (50 units for HR, $20 * 3$ for PA), a mixed model ANOVA was used, followed by post hoc comparisons of the LSD test (for 50 units of HR) and the Bonferroni test (for PA), as well as under the following conditions: initial units for HR and PA (four first 10-second intervals); latency of minimum for HR; latency of

maximum for HR; 8 units from 9 to 16, when differences between groups were most pronounced.

Results

Group differences in HR and PA (based on not-normalized values)

We compared the not-normalized means of HR and PA between the OCD group and the control group and found that the OCD group showed greater PA [$F(1, 60) = 8.586, p = 0.0048$] and higher HR [$F(1, 60) = 7.469, p = 0.0083$] compared to the control group, regardless of the experimental block and type of stimuli. In both groups, not-normalized HR values did not differ significantly between experimental blocks, but PA showed a significant decrease from the 1-st to the 2-nd and 3-rd blocks: [$F(2, 120) = 11.361, p < 0.0001$; post hoc comparison between the 1-st and 2-nd blocks $p = 0.0083$ and between the 1st and 3-rd blocks $p < 0.0001$]. In addition, PA was significantly lower for neutral stimuli compared to positive and negative stimuli: [$F(2, 120) = 370.26, p < 0.0001$; post hoc comparison $p < 0.0001$]. There were no interaction effects between group, block, and stimulus valence factors.

Dynamics of HR (based on normalized values)

HR dynamics in both groups

In each experimental block, a distinct dynamics of HR was observed, which, although it was more stable in the control group, was also recorded in the OCD group. This pattern had significant differences from the first to the third experimental block of the antisaccade task.

Each block began with an elevated HR, which gradually decreased and reached a minimum point approximately 1 minute after the start of the block.

ANOVA showed significant dynamic changes in HR over 50 10-second intervals: [$F(49, 2940) = 8.022, p < 0.0001$]. ANOVA also confirmed significant dynamic changes in HR for three parameters: initial units (average HR in the first 4 units), the latency of the minimum and latency of the maximum. In particular, the latency of the minimum of HR differed significantly between the first and third

experimental blocks, with the latency in the first block being significantly longer than in the third in both groups [$F(2, 120) = 14.144, p < 0.0001$]. After the minimum, HR increased until it reached a maximum at the end of the block. The latency of the maximum in healthy participants typically occurred between 7 and 8 minutes, and was significantly higher in healthy participants in the third block compared to the first [$F(2, 120) = 10.753, p < 0.0001$]. This effect was not observed in the OCD group.

Intergroup differences in HR dynamics

In the initial units of the first block (the first four units), the normalized HR in the control group was significantly higher compared to the group with OCD: [$F(1, 60) = 6.372, p = 0.014$; post hoc comparison $p < 0.05$]. The latency of the minimum HR in the control group was significantly shorter compared to the OCD group in the last block: [$F(1, 60) = 4.983, p = 0.0365$; post hoc comparison $p < 0.05$]. ANOVA with levels within 50 units revealed group differences (post hoc comparison $p < 0.05$), which are indicated in yellow (Fig. 8a).

In the control group, we observed a significantly longer latency for the appearance of the minimum HR in the first experimental block. Conversely, in the third block, the latency of minimum was noticeably shorter in the control group (Fig. 8b). There were no significant differences in latency between groups in the second block. Regarding intragroup differences between blocks, healthy volunteers showed a significant decrease in HR peak latency from the first to the third block. In contrast, patients with OCD did not show any differences in latency between blocks (mixed group * block effect [$F(2, 120) = 7.784, p = 0.0006$]; post hoc comparison between blocks: $p = 0.007$ for control group, $p = 0.31$ for the OCD group).

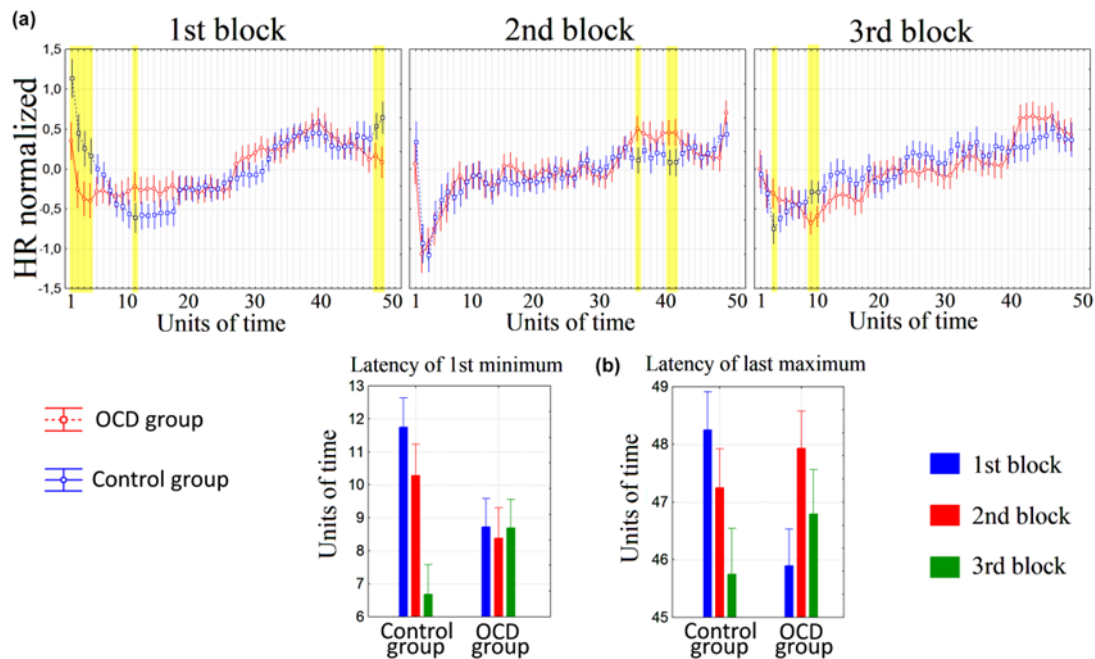


Figure 8. The heart rate (HR) dynamics in three experimental blocks. (a) The HR dynamics for 50-time units in two groups of participants; yellow marker lines – the significant group differences after LSD correction ($p < 0.05$) and (b) the latencies (in units of time) of the first minimum and last maximum.

Dynamics of PA in both groups

The dynamics of PA from experimental blocks 1 to 3 showed that both groups had similar trends. It is noteworthy that in the middle part of block 3, the PA had significantly lower mean values for all types of stimuli compared to other blocks (main block effect for 8 units from 9 to 16: $[F(2, 120) = 19.387, p < 0.0001]$).

PA in the initial units (1–4) was significantly higher in the first block compared to the rest in both groups $[F(2, 120) = 37.898, p < 0.0001]$.

Intergroup differences in the dynamics of PA

ANOVA analysis revealed significant group differences in the initial units (1–4) in PA between experimental blocks. Specifically, the control group showed greater PA at the beginning of each experimental block $[F(1, 60) = 4.494, p = 0.0322]$.

In the middle of experimental blocks 1 and 2 (from 3.5 to 6.5 minutes from the beginning of the block), PA was significantly greater in the OCD group to negative stimuli compared to the control group. During the third block, a similar

difference was found only for negative (Fig. 9a) and neutral stimuli (Fig. 9c) and was not found for positive stimuli (Fig. 9b). ANOVA for 8 units (from 9 to 16) followed by post hoc comparisons ($p = 0.003$) confirmed significant group differences (group*block effect [$F(2, 120) = 5.482, p = 0.0052$]).

Finally, we compared the temporal dynamics of PA from blocks 1 to 3 between groups and found that, in contrast to the control group, patients with OCD did not show a significant decrease in PA in the last experimental block compared to the first when neutral stimuli were presented (group effect* block [$F(1, 60) = 15.048, p = 0.0003$]; post hoc comparison $p = 0.0085$ in the control group).

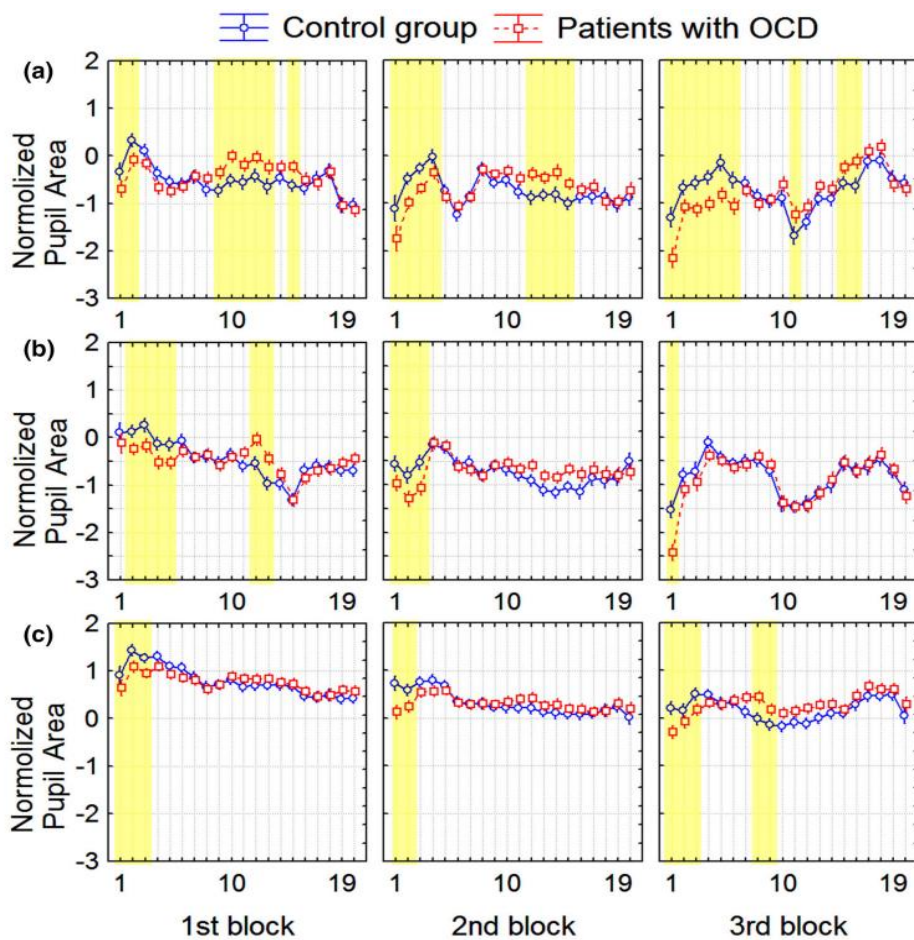


Figure 9. The pupil area dynamics in three experimental blocks for two groups of participants; yellow marker lines – the significant group differences after LSD correction ($p < 0.05$). The abscissa – the time units: the pupil area during each stimulus (only for neutral it was averaged for 3 stimuli). (a) unpleasant images; (b) pleasant images; and (c) neutral images.

Conclusions

The OCD group showed greater PA and higher HR values (based on not-normalized data) during 3 blocks of the antisaccade task, suggesting increased sympathetic tone in OCD in general.

The obtained results of HR and PA, and their dynamics, testify in favor of the hypothesis of a decrease in the physiological flexibility of the ANS in OCD. At the initial stages of the first block of the antisaccade task, a significantly lower HR value was observed in the OCD group compared to the control group. An increased HR at the beginning of any cognitive-emotional load is a typical reaction of the ANS to adapt to it. A lower HR may indicate a reduced level of mobility and adaptability of the ANS, which does not allow timely initiation of adaptation to an increase in load through temporary activation of sympathetic tone.

The latency of the minimum gradually decreased in the control group from block 1 to block 3, while in the OCD group this parameter remained practically unchanged. This suggests that over time from the start of the task, the control group experienced adaptation of the ANS, while in OCD there were no adaptive changes in the ANS to the load from block to block.

Patients with OCD did not show a significant decrease in PA from the 1st to the last experimental blocks, compared to the control group. These results are consistent with previous research showing that patients with severe OCD symptoms tend to exhibit greater rigidity in ANS responses.

At the beginning of each block, healthy volunteers showed significantly greater PA for all types of stimuli. However, in contrast to the control group, the greater increase in PA in the middle part of each block in the OCD group was more pronounced in response to negative stimuli than to other types of stimuli. The observed increase in the ANS response, reflected in pronounced changes in mental health to negative stimuli, may be associated with a violation of the mechanisms of emotional regulation and general maladaptation of the ANS in OCD.

3. CONCLUSION

The antisaccade «overlap» design task with stimuli of different emotional valence (neutral, positive and negative) can be used to study the influence of emotional regulation on executive functions in mental disorders.

In our work, we primarily determined the optimal scenario for the antisaccade task in the form of an «overlap» design. Comparison of blocks in both groups showed that eye movements in the «overlap» block differed from the «step» and «gap» blocks. Express and regular error rate, the average amplitude of express and regular errors, latency and velocity of erroneous antisaccades were higher when performing tasks in the «overlap» scenario than in the «step» and «gap» scenarios. Moreover, the values of the average latency of express errors and the average velocity of express errors were also the highest for the «overlap» scenario.

Having determined the optimal design of the antisaccade task, we applied it to patients with OCD and healthy volunteers. Our finding of increased error rates in response to negative stimuli in patients with OCD compared with healthy controls suggests that the effect of negative stimuli on inhibitory control may play an important role in OCD. This effect may be related to emotional dysregulation in OCD. Moreover, our results also show that response latencies to negative and neutral stimuli were significantly longer than to positive stimuli in the OCD group. It can be assumed that participants with OCD are stuck on negative stimuli, and therefore perform tasks with emotionally negative stimuli more slowly. Obsessive-compulsive triggers can cause decreased attention to relevant information, increased attention to irrelevant information, and decreased ability to suppress it. This confirms our finding that patients with OCD have higher latency to make correct antisaccades in response to negative images after fixating on them. Also in our study, a higher latency to neutral stimuli was observed than to positive ones in the OCD group. However, we cannot conclude that general inhibitory control is impaired because there were no statistical differences in error rates between the OCD group and the healthy control group for neutral stimuli.

In parallel to the second study, we studied the features of HR and PA, as well as their dynamics during all three blocks of the antisaccade task in relation to the OCD group and healthy volunteers. Increased HR and increased PA in patients with OCD compared to healthy volunteers may indicate increased tone of the sympathetic nervous system in OCD in general. At the same time, the lower value of HR and PA at the beginning of each block in the OCD group compared to the control group may indicate a reduced level of mobility and adaptability of the ANS, which does not allow timely initiation of adaptation to an increase in load through temporary activation of sympathetic tone. An increased HR at the beginning of any cognitive-emotional load is a typical reaction of the ANS to adapt to it. The reduced physiological flexibility of the ANS and its maladaptation in OCD can be evidenced by the results of a study of HR dynamics in the form of the absence of a gradual decrease in the latency of the minimum from the first to the third block. This may indicate that over time there were no adaptive changes in the ANS to the load from block to block in OCD. A greater increase in PA in the middle part of each block to negative stimuli in the OCD group compared to the control group may also confirm a violation of the mechanisms of emotional regulation and general maladaptation of the ANS in OCD.

In our work, we showed that negative emotional stimuli affect the functions of inhibitory control in OCD, possibly through a shift of attention towards negative stimuli, which in turn is associated with a deterioration in the physiological adaptation of the ANS to load, especially to emotionally significant ones.

REFERENCES

- Abbott, D., Shirali, Y., Haws, J. K., & Lack, C. W. (2017). Biobehavioral assessment of the anxiety disorders: Current progress and future directions. *World Journal of Psychiatry, 7*(3), 133–147. <https://doi.org/10.5498/wjp.v7.i3.133>
- Agam, Y., Greenberg, J. L., Isom, M., Falkenstein, M. J., Jenike, E., Wilhelm, S., & Manoach, D. S. (2014). Aberrant error processing in relation to symptom severity in obsessive–compulsive disorder: A multimodal neuroimaging study. *NeuroImage: Clinical, 5*, 141–151. <https://doi.org/10.1016/j.nicl.2014.06.002>
- Agam, Y., Joseph, R. M., Barton, J. J. S., & Manoach, D. S. (2010). Reduced cognitive control of response inhibition by the anterior cingulate cortex in autism spectrum disorders. *NeuroImage, 52*(1), 336–347. <https://doi.org/10.1016/j.neuroimage.2010.04.010>
- Armstrong, T., Olatunji, B. O., Sarawgi, S., & Simmons, C. (2010). Orienting and maintenance of gaze in contamination fear: Biases for disgust and fear cues. *Behaviour Research and Therapy, 48*(5), 402–408. <https://doi.org/10.1016/j.brat.2010.01.002>
- Armstrong, T., Sarawgi, S., & Olatunji, B. O. (2012). Attentional bias toward threat in contamination fear: Overt components and behavioral correlates. *Journal of Abnormal Psychology, 121*(1), 232–237. <https://doi.org/10.1037/a0024453>
- Bannon, S., Gonsalvez, C. J., & Croft, R. J. (2008). Processing impairments in OCD: It is more than inhibition! *Behaviour Research and Therapy, 46*(6), 689–700. <https://doi.org/10.1016/j.brat.2008.02.006>
- Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: Behavioral and neural basis of response control. *Progress in Neurobiology, 108*, 44–79. <https://doi.org/10.1016/j.pneurobio.2013.06.005>
- Basel, D., Hallel, H., Dar, R., & Lazarov, A. (2023). Attention allocation in OCD: A systematic review and meta-analysis of eye-tracking-based research. *Journal of Affective Disorders, 324*, 539–550. <https://doi.org/10.1016/j.jad.2022.12.141>

Beck, Emery G., & Greenberg R. L. (1985). *Anxiety disorders and phobias: A cognitive perspective*. Basic Books.

Bedford, C. E., Nakamura, Y., Marchand, W. R., & Garland, E. L. (2022). Heightened autonomic reactivity to negative affective stimuli among active duty soldiers with PTSD and opioid-treated chronic pain. *Psychiatry Research*, *309*, 114394. <https://doi.org/10.1016/j.psychres.2022.114394>

Benzina, N., Mallet, L., Burguière, E., N'Diaye, K., & Pelissolo, A. (2016). Cognitive Dysfunction in Obsessive-Compulsive Disorder. *Current Psychiatry Reports*, *18*(9), 80. <https://doi.org/10.1007/s11920-016-0720-3>

Bey, K., Lennertz, L., Grützmann, R., Heinzl, S., Kaufmann, C., Klawohn, J., Riesel, A., Meyhöfer, I., Ettinger, U., Kathmann, N., & Wagner, M. (2018). Impaired Antisaccades in Obsessive-Compulsive Disorder: Evidence From Meta-Analysis and a Large Empirical Study. *Frontiers in Psychiatry*, *9*, 284. <https://doi.org/10.3389/fpsy.2018.00284>

Blekic, W., Wauthia, E., Kornacka, M., Kandana Arachchige, K., Lefebvre, L., & Rossignol, M. (2021). Eye-tracking exploration of inhibitory control in post-traumatic stress disorder: An emotional antisaccade paradigm. *European Journal of Psychotraumatology*, *12*(1), 1909281.

Bohne, A., Keuthen, N. J., Tuschen-Caffier, B., & Wilhelm, S. (2005). Cognitive inhibition in trichotillomania and obsessive-compulsive disorder. *Behaviour Research and Therapy*, *43*(7), 923–942. <https://doi.org/10.1016/j.brat.2004.06.014>

Bradley, M. C., Hanna, D., Wilson, P., Scott, G., Quinn, P., & Dyer, K. F. W. (2016). Obsessive-compulsive symptoms and attentional bias: An eye-tracking methodology. *Journal of Behavior Therapy and Experimental Psychiatry*, *50*, 303–308. <https://doi.org/10.1016/j.jbtep.2015.10.007>

Brooks, S. J., & Stein, D. J. (2015). A systematic review of the neural bases of psychotherapy for anxiety and related disorders. *Dialogues in Clinical Neuroscience*, *17*(3), 261–279. <https://doi.org/10.31887/DCNS.2015.17.3/sbrooks>

Buccelletti, E., Gilardi, E., Scaini, E., Galiuto, L., Persiani, R., Biondi, A., Basile, F., & Silveri, N. G. (2009). Heart rate variability and myocardial infarction: Systematic literature review and metanalysis. *European Review for Medical and Pharmacological Sciences*, *13*(4), 299–307.

Carnac, T. (2022). Schizophrenia Hypothesis: Autonomic Nervous System Dysregulation of Fetal and Adult Immune Tolerance. *Frontiers in Systems Neuroscience*, *16*, 844383. <https://doi.org/10.3389/fnsys.2022.844383>

Coe, B. C., & Munoz, D. P. (2017). Mechanisms of saccade suppression revealed in the anti-saccade task. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *372*(1718), 20160192. <https://doi.org/10.1098/rstb.2016.0192>

Crawford, T. J., Haeger, B., Kennard, C., Reveley, M. A., & Henderson, L. (1995). Saccadic abnormalities in psychotic patients. II. The role of neuroleptic treatment. *Psychological Medicine*, *25*(3), 473–483. <https://doi.org/10.1017/S0033291700033390>

Dalley, J. W., Everitt, B. J., & Robbins, T. W. (2011). Impulsivity, Compulsivity, and Top-Down Cognitive Control. *Neuron*, *69*(4), 680–694. <https://doi.org/10.1016/j.neuron.2011.01.020>

Fernández De La Cruz, L., Landau, D., Iervolino, A. C., Santo, S., Pertusa, A., Singh, S., & Mataix-Cols, D. (2013). Experiential avoidance and emotion regulation difficulties in hoarding disorder. *Journal of Anxiety Disorders*, *27*(2), 204–209. <https://doi.org/10.1016/j.janxdis.2013.01.004>

Fineberg, N. A., Apergis-Schoute, A. M., Vaghi, M. M., Banca, P., Gillan, C. M., Voon, V., Chamberlain, S. R., Cinosi, E., Reid, J., Shahper, S., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2018). Mapping Compulsivity in the DSM-5 Obsessive Compulsive and Related Disorders: Cognitive Domains, Neural Circuitry, and Treatment. *International Journal of Neuropsychopharmacology*, *21*(1), 42–58. <https://doi.org/10.1093/ijnp/pyx088>

Funch Uhre, V., Melissa Larsen, K., Marc Herz, D., Baaré, W., Katrine Pagsberg, A., & Roman Siebner, H. (2022). Inhibitory control in obsessive

compulsive disorder: A systematic review and activation likelihood estimation meta-analysis of functional magnetic resonance imaging studies. *NeuroImage: Clinical*, 36, 103268. <https://doi.org/10.1016/j.nicl.2022.103268>

Goto, Y., Hatakeyama, K., Kitama, T., Sato, Y., Kanemura, H., Aoyagi, K., Sugita, K., & Aihara, M. (2010). Saccade eye movements as a quantitative measure of frontostriatal network in children with ADHD. *Brain and Development*, 32(5), 347–355. <https://doi.org/10.1016/j.braindev.2009.04.017>

Gramzow, R. H., Willard, G., & Mendes, W. B. (2008). Big tales and cool heads: Academic exaggeration is related to cardiac vagal reactivity. *Emotion*, 8(1), 138–144. <https://doi.org/10.1037/1528-3542.8.1.138>

Green, J. F., & King, D. J. (1998). The effects of chlorpromazine and lorazepam on abnormal antisaccade and no-saccade distractibility. *Biological Psychiatry*, 44(8), 709–715. [https://doi.org/10.1016/S0006-3223\(97\)00452-6](https://doi.org/10.1016/S0006-3223(97)00452-6)

Gürsel, D. A., Avram, M., Sorg, C., Brandl, F., & Koch, K. (2018). Frontoparietal areas link impairments of large-scale intrinsic brain networks with aberrant fronto-striatal interactions in OCD: A meta-analysis of resting-state functional connectivity. *Neuroscience & Biobehavioral Reviews*, 87, 151–160. <https://doi.org/10.1016/j.neubiorev.2018.01.016>

Hakvoort Schwerdtfeger, R. M., Alahyane, N., Brien, D. C., Coe, B. C., Stroman, P. W., & Munoz, D. P. (2013). Preparatory neural networks are impaired in adults with attention-deficit/hyperactivity disorder during the antisaccade task. *NeuroImage: Clinical*, 2, 63–78. <https://doi.org/10.1016/j.nicl.2012.10.006>

Hazari, N., Narayanaswamy, J., & Venkatasubramanian, G. (2019). Neuroimaging findings in obsessive–compulsive disorder: A narrative review to elucidate neurobiological underpinnings. *Indian Journal of Psychiatry*, 61(7), 9. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_525_18

Herzog, S. A., & Brakoulias, V. (2022). The Role of Neurophysiological Biomarkers in Obsessive-Compulsive Disorder. *Current Medicinal Chemistry*, 29(35), 5584–5594. <https://doi.org/10.2174/0929867329666211217094941>

Hu, Y., Liao, R., Chen, W., Kong, X., Liu, J., Liu, D., Maguire, P., Zhou, S., & Wang, D. (2020). Investigating behavior inhibition in obsessive-compulsive disorder: Evidence from eye movements. *Scandinavian Journal of Psychology*, *61*(5), 634–641. <https://doi.org/10.1111/sjop.12620>

Hutton, S. B., & Ettinger, U. (2006). The antisaccade task as a research tool in psychopathology: A critical review. *Psychophysiology*, *43*(3), 302–313. <https://doi.org/10.1111/j.1469-8986.2006.00403.x>

Jaafari, N., Rigalleau, F., Rachid, F., Delamillieure, P., Millet, B., Olié, J.-P., Gil, R., Rotge, J.-Y., & Vibert, N. (2011). A critical review of the contribution of eye movement recordings to the neuropsychology of obsessive compulsive disorder: Eye movements in obsessive compulsive disorder. *Acta Psychiatrica Scandinavica*, *124*(2), 87–101. <https://doi.org/10.1111/j.1600-0447.2011.01721.x>

Karpinski, M., Mattina, G. F., & Steiner, M. (2017). Effect of Gonadal Hormones on Neurotransmitters Implicated in the Pathophysiology of Obsessive-Compulsive Disorder: A Critical Review. *Neuroendocrinology*, *105*(1), 1–16. <https://doi.org/10.1159/000453664>

Kennard, C. (2011). Disorders of higher gaze control. In *Handbook of Clinical Neurology* (Vol. 102, pp. 379–402). Elsevier. <https://doi.org/10.1016/B978-0-444-52903-9.00020-0>

Khayrullina, G. M., Moiseeva, V. V., & Martynova, O. V. (2022). Specific Aspects of Eye Movement Reactions as Markers of Cognitive Control Disorders in Patients with Obsessive-Compulsive Disorder (Review). *Sovremennyye Tehnologii v Medicine*, *14*(2), 80. <https://doi.org/10.17691/stm2022.14.2.08>

Kloft, L., Reuter, B., Riesel, A., & Kathmann, N. (2013). Impaired volitional saccade control: First evidence for a new candidate endophenotype in obsessive-compulsive disorder. *European Archives of Psychiatry and Clinical Neuroscience*, *263*(3), 215–222. <https://doi.org/10.1007/s00406-012-0331-x>

Lennertz, L., Rampacher, F., Vogeley, A., Schulze-Rauschenbach, S., Pukrop, R., Ruhrmann, S., Klosterkötter, J., Maier, W., Falkai, P., & Wagner, M. (2012). Antisaccade performance in patients with obsessive-compulsive disorder and

unaffected relatives: Further evidence for impaired response inhibition as a candidate endophenotype. *European Archives of Psychiatry and Clinical Neuroscience*, 262(7), 625–634. <https://doi.org/10.1007/s00406-012-0311-1>

Levine, L. E., Waite, B. M., & Bowman, L. L. (2007). Electronic Media Use, Reading, and Academic Distractibility in College Youth. *CyberPsychology & Behavior*, 10(4), 560–566. <https://doi.org/10.1089/cpb.2007.9990>

Leuchs, L., Schneider, M., & Spoormaker, V. I. (2019). Measuring the conditioned response: A comparison of pupillometry, skin conductance, and startle electromyography. *Psychophysiology*, 56(1), e13283. <https://doi.org/10.1111/psyp.13283>

Liang, C.-W. (2018). Attentional control deficits in social anxiety: Investigating inhibition and shifting functions using a mixed antisaccade paradigm. *Journal of Behavior Therapy and Experimental Psychiatry*, 60, 46–52. <https://doi.org/10.1016/j.jbtep.2018.03.004>

Lynch, G., King, D. J., Green, J. F., Byth, W., & Wilson-Davis, K. (1997). The effects of haloperidol on visual search, eye movements and psychomotor performance. *Psychopharmacology*, 133(3), 233–239. <https://doi.org/10.1007/s002130050396>

Maruff, P., Purcell, R., Tyler, P., Pantelis, C., & Currie, J. (1999). Abnormalities of internally generated saccades in obsessive–compulsive disorder. *Psychological Medicine*, 29(6), 1377–1385. <https://doi.org/10.1017/S0033291799008843>

Mikels, J. A., Fredrickson, B. L., Larkin, G. R., Lindberg, C. M., Maglio, S. J., & Reuter-Lorenz, P. A. (2005). Emotional category data on images from the international affective picture system. *Behavior Research Methods*, 37(4), 626–630. <https://doi.org/10.3758/BF03192732>

Milad, M. R., Furtak, S. C., Greenberg, J. L., Keshaviah, A., Im, J. J., Falkenstein, M. J., Jenike, M., Rauch, S. L., & Wilhelm, S. (2013). Deficits in Conditioned Fear Extinction in Obsessive-Compulsive Disorder and

Neurobiological Changes in the Fear Circuit. *JAMA Psychiatry*, 70(6), 608.
<https://doi.org/10.1001/jamapsychiatry.2013.914>

Morein-Zamir, S., Pappmeyer, M., Gillan, C. M., Crockett, M. J., Fineberg, N. A., Sahakian, B. J., & Robbins, T. W. (2013). Punishment promotes response control deficits in obsessive-compulsive disorder: Evidence from a motivational go/no-go task. *Psychological Medicine*, 43(2), 391–400.
<https://doi.org/10.1017/S0033291712001018>

Munoz, D. P., Armstrong, I. T., Hampton, K. A., & Moore, K. D. (2003). Altered Control of Visual Fixation and Saccadic Eye Movements in Attention-Deficit Hyperactivity Disorder. *Journal of Neurophysiology*, 90(1), 503–514.
<https://doi.org/10.1152/jn.00192.2003>

Nakao, T., Okada, K., & Kanba, S. (2014). Neurobiological model of obsessive-compulsive disorder: Evidence from recent neuropsychological and neuroimaging findings. *Psychiatry and Clinical Neurosciences*, 68(8), 587–605.
<https://doi.org/10.1111/pcn.12195>

Narayanaswamy, J. C., Subramaniam, A., Bose, A., Agarwal, S. M., Kalmady, S. V., Jose, D., Joseph, B., Shivakumar, V., Hutton, S. B., Venkatasubramanian, G., & Reddy, Y. C. J. (2021). Antisaccade task performance in obsessive-compulsive disorder and its clinical correlates. *Asian Journal of Psychiatry*, 57, 102508.
<https://doi.org/10.1016/j.ajp.2020.102508>

Nigg, J. T. (2013). Attention deficits and hyperactivity-impulsivity: What have we learned, what next? *Development and Psychopathology*, 25(4pt2), 1489–1503.
<https://doi.org/10.1017/S0954579413000734>

Norman, L. J., Taylor, S. F., Liu, Y., Radua, J., Chye, Y., De Wit, S. J., Huysen, C., Karahanoglu, F. I., Luks, T., Manoach, D., Mathews, C., Rubia, K., Suo, C., Van Den Heuvel, O. A., Yücel, M., & Fitzgerald, K. (2019). Error Processing and Inhibitory Control in Obsessive-Compulsive Disorder: A Meta-analysis Using Statistical Parametric Maps. *Biological Psychiatry*, 85(9), 713–725.
<https://doi.org/10.1016/j.biopsych.2018.11.010>

Olbrich, H., Jahn, I., Stengler, K., Seifritz, E., & Colla, M. (2022). Heart rate variability in obsessive compulsive disorder in comparison to healthy controls and as predictor of treatment response. *Clinical Neurophysiology*, *138*, 123–131. <https://doi.org/10.1016/j.clinph.2022.02.029>

Park, J. E., Kang, S.-H., Lee, J. Y., Won, S.-D., So, H. S., Choi, J. H., Kim, C.-H., & Yoon, I. Y. (2019). Clinical utility of heart rate variability during Head-up tilt test in subjects with chronic posttraumatic stress disorder. *Psychiatry Research*, *272*, 100–105. <https://doi.org/10.1016/j.psychres.2018.12.035>

Pilarczyk, J., & Kuniecki, M. (2014). Emotional content of an image attracts attention more than visually salient features in various signal-to-noise ratio conditions. *Journal of Vision*, *14*(12), 4–4. <https://doi.org/10.1167/14.12.4>

Pöhlchen, D., Priouret, M., Kraft, M. S., Binder, F. P., Gürsel, D. A., Berberich, G., BeCOME working group, Koch, K., & Spoormaker, V. I. (2021). Examining Differences in Fear Learning in Patients With Obsessive-Compulsive Disorder With Pupillometry, Startle Electromyography and Skin Conductance Responses. *Frontiers in Psychiatry*, *12*, 730742. <https://doi.org/10.3389/fpsyt.2021.730742>

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychology*, *74*(2), 116–143. <https://doi.org/10.1016/j.biopsycho.2006.06.009>

Rachman S. & Hodgson R. (1980). *Obsessions and compulsions*. Prentice-Hall.

Reilly, J. L., Lencer, R., Bishop, J. R., Keedy, S., & Sweeney, J. A. (2008). Pharmacological treatment effects on eye movement control. *Brain and Cognition*, *68*(3), 415–435. <https://doi.org/10.1016/j.bandc.2008.08.026>

Roecklein, K., Wong, P., Ernecoff, N., Miller, M., Donofry, S., Kamarck, M., Wood-Vasey, W. M., & Franzen, P. (2013). The post illumination pupil response is reduced in seasonal affective disorder. *Psychiatry Research*, *210*(1), 150–158. <https://doi.org/10.1016/j.psychres.2013.05.023>

Safonova, V. R., & Shalamova, E. Y. (2013). *Parameters of heart rate variability in female students of northern medical school under exam stress*. *20*(8), 11–16.

Salkovskis P. M. & McGuire J. (2003). Cognitive-behavioural theory of OCD. In *Obsessive-compulsive Disorder: Theory, research and treatment* (Vol. 65, p. 59e78). Chichester: Wiley.

Saxena, S., Brody, A. L., Schwartz, J. M., & Baxter, L. R. (1998). Neuroimaging and frontal-subcortical circuitry in obsessive-compulsive disorder. *The British Journal of Psychiatry. Supplement*, 35, 26–37.

See, C. C. H., Tan, J. M., Tan, V. S. Y., & Sündermann, O. (2022). A systematic review on the links between emotion regulation difficulties and obsessive-compulsive disorder. *Journal of Psychiatric Research*, 154, 341–353. <https://doi.org/10.1016/j.jpsychires.2022.07.023>

Sekaninová, N., Mestanik, M., Mestanikova, A., Hamrakova, A., & Tonhajzerova, I. (2019). Novel approach to evaluate central autonomic regulation in attention deficit/hyperactivity disorder (ADHD). *Physiological Research*, 531–545. <https://doi.org/10.33549/physiolres.934160>

Siqueiros Sanchez, M., Falck-Ytter, T., Kennedy, D. P., Bölte, S., Lichtenstein, P., D’Onofrio, B. M., & Pettersson, E. (2020). Volitional eye movement control and ADHD traits: A twin study. *Journal of Child Psychology and Psychiatry*, 61(12), 1309–1316. <https://doi.org/10.1111/jcpp.13210>

Stern, E. R., & Taylor, S. F. (2014). Cognitive Neuroscience of Obsessive-Compulsive Disorder. *Psychiatric Clinics of North America*, 37(3), 337–352. <https://doi.org/10.1016/j.psc.2014.05.004>

Stogios, N., Gdanski, A., Gerretsen, P., Chintoh, A. F., Graff-Guerrero, A., Rajji, T. K., Remington, G., Hahn, M. K., & Agarwal, S. M. (2021). Autonomic nervous system dysfunction in schizophrenia: Impact on cognitive and metabolic health. *Npj Schizophrenia*, 7(1), 22. <https://doi.org/10.1038/s41537-021-00151-6>

Summerfeldt, L. J., Hood, K., Antony, M. M., Richter, M. A., & Swinson, R. P. (2004). Impulsivity in obsessive-compulsive disorder: Comparisons with other anxiety disorders and within tic-related subgroups. *Personality and Individual Differences*, 36(3), 539–553. [https://doi.org/10.1016/S0191-8869\(03\)00113-2](https://doi.org/10.1016/S0191-8869(03)00113-2)

Taylor, A. J. G., & Hutton, S. B. (2009). The effects of task instructions on pro and antisaccade performance. *Experimental Brain Research*, *195*(1), 5–14. <https://doi.org/10.1007/s00221-009-1750-4>

Thayer, J. F., Åhs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience & Biobehavioral Reviews*, *36*(2), 747–756. <https://doi.org/10.1016/j.neubiorev.2011.11.009>

Toffolo, M. B. J., Van Den Hout, M. A., Engelhard, I. M., Hooge, I. T. C., & Cath, D. C. (2016). Patients With Obsessive-Compulsive Disorder Check Excessively in Response to Mild Uncertainty. *Behavior Therapy*, *47*(4), 550–559. <https://doi.org/10.1016/j.beth.2016.04.002>

Van Den Berg, M., Maas, J., Muller, R., Braun, A., Kaandorp, W., Van Lien, R., Van Poppel, M., Van Mechelen, W., & Van Den Berg, A. (2015a). Autonomic Nervous System Responses to Viewing Green and Built Settings: Differentiating Between Sympathetic and Parasympathetic Activity. *International Journal of Environmental Research and Public Health*, *12*(12), 15860–15874. <https://doi.org/10.3390/ijerph121215026>

Van Den Berg, M., Maas, J., Muller, R., Braun, A., Kaandorp, W., Van Lien, R., Van Poppel, M., Van Mechelen, W., & Van Den Berg, A. (2015b). Autonomic Nervous System Responses to Viewing Green and Built Settings: Differentiating Between Sympathetic and Parasympathetic Activity. *International Journal of Environmental Research and Public Health*, *12*(12), 15860–15874. <https://doi.org/10.3390/ijerph121215026>

Van Der Wee, N. J., Hardeman, H. H., Ramsey, N. F., Raemaekers, M., Van Megen, H. J., Denys, D. A., Westenberg, H. G., & Kahn, R. S. (2006). Saccadic abnormalities in psychotropic-naive obsessive–compulsive disorder without comorbidity. *Psychological Medicine*, *36*(9), 1321–1326. <https://doi.org/10.1017/S0033291706007926>

Vasanov A. Yu., Marchenko O.P., Mashanlo A.S. (2011). Approbation of standart measured of emotional pictures from IAPS on Russian sample. *Experimental Psychology*, 4(3), 126–132.

Vasanov A. Yu., Marchenko O.P., Sevostianova M.S. (2013). Selection of culture-specific emotion evocative pictures for experimental studies. *Experimental Psychology*, 6(4), 105-114.

Wang, C., & Munoz, D. P. (2014). Modulation of stimulus contrast on the human pupil orienting response. *European Journal of Neuroscience*, 40(5), 2822–2832. <https://doi.org/10.1111/ejn.12641>

WHO. (1983). *International classification of diseases 10th revision (ICD-10)*. World Health Organization (WHO). <https://mkb-10.com/>;

WHO. (1999). *The “newly defined” burden of mental problems*.

WHO. (2019). *International classification of diseases 10th revision (ICD-10)*. World Health Organization (WHO). <https://icd.who.int/en>

WHO. (2022). *International classification of diseases 11th revision (ICD-11)*. World Health Organization (WHO). <https://icd.who.int/en>

Williams, MacLeod C. M., Watts F. N., & Mathews A. (1997). *Cognitive psychology and emotional disorders*. Wiley.

Zetsche, U., Rief, W., Westermann, S., & Exner, C. (2015). Cognitive deficits are a matter of emotional context: Inflexible strategy use mediates context-specific learning impairments in OCD. *Cognition and Emotion*, 29(2), 360–371. <https://doi.org/10.1080/02699931.2014.911144>