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a) **The article title:**

" Social phobia"

Social phobia

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Abstract

Social anxiety disorder (social phobia) is an irrational fear of being observed and judged by other people in various social settings. The individual fears that he or she will act in a way that will be humiliating or embarrassing. It is often a chronic, disabling condition that is characterized by a phobic avoidance of most social situations. Social anxiety disorder is the most frequent anxiety disorder (10-15%), which occurs in two subtypes – generalized and specific (discrete). It is a disorder that occurs during adolescence and reflects negatively to the quality of life of an individual. Neurobiological basis of this disorder still is not explored. The disorder is frequently burdened with comorbidity with other anxiety disorders, depression and alcohol and drug dependence. In psychotherapeutic treatment of the disorder only cognitive-behavioral techniques are desirable, and the best results are achieved in combination with pharmacotherapy. The medicaments of choice in treatment of social anxiety disorder are selective serotonin reuptake inhibitors. Anxiolytics should be used only as a supplementary in the acute phase. Treatment of social anxiety disorder should last at least 3 months up to one year.

Key words: social anxiety disorder; social phobia; comorbidity; treatment; selective serotonin reuptake inhibitors; anxiolytics

Social phobia

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Introduction

Social anxiety disorder (social phobia) is an irrational fear of being exposed to observation and judgment by other people in various social settings. It is manifested as a fear of public speaking, giving lectures and TV statements, giving opinions at meetings; meeting important persons, showing knowledge and skills on examinations, eating in the presence of unfamiliar people, etc. The person is afraid of being embarrassed and humiliated in public by his or her clumsiness, inexperience or ignorance. Fear occurs when an individual is confronted with a group of other people in social settings in which he or she becomes the center of their attention. If a person is forced to be in a phobic situation, he or she experiences strong anxiety symptoms (blushing, sweating, trembling and speech blocks), together with negative cognitive interpretations (his or her performance will be judged as stupid, inadequate and dull). The person is aware of his or her anxiousness and accompanying body signs that he or she believes can easily be noticed by others; it results in a fear from fear, which intensifies the original fear, and panic may occur. Such a person develops a strong anticipating anxiety of being confronted with phobic situations, and tries to avoid them if possible. It has a negative influence to his or her social activities and relationships, what results in

reduction of a quality of life. Social anxiety disorder is the most frequent anxiety disorder (10 – 15%) and is, as such, often unrecognized as the cause of failure in school and career, divorce, inexplicable rejections of good business offers, a social life, alcoholism, drug dependence, and more other forms of life failures that resulted from avoiding phobic situations. In the best case they are recognized as persons with mental disorders, or otherwise they are disqualified as incompetent, inept, less worthy, and with high chances to become "the residue" of the busy, commercially oriented society. Even today, such persons usually ask for medical treatment of secondary mental disturbances that resulted from unsuccessful avoiding behavior, and clinicians treat general anxiety, panic attacks, depression, alcoholism and drug dependence, not recognizing social anxiety disorder as the main cause. The problem of nonrecognition of social anxiety disorder occurs all over the world. According to studies, social anxiety disorder occurs between 13,3% in USA (1) and 14,4% in Europe (2), but the recognition of the disorder in practice is very low. Only about 5% of persons with this disorder ask for help (3), and when they do, only a quarter of them are diagnosed this disorder (4, 5).

Definition and subtypes of social anxiety disorder

Reasonable anxiety and shyness are normal, ubiquitous, and, for social functioning, desirable feelings. Only when their intensity is too high and interferes with social functioning, they become psychiatric condition. Therefore, to make proper diagnosis, we need diagnostic criteria. The criteria enable us to put a line between general anxiety and social anxiety disorder on one hand, and between this and other mental disorders on the other hand. In both classifications (DSM-IV and ICD-10)

the main characteristic of social anxiety disorder is a fear of a person to be judged and observed by other people, and he or she expects that results of such a judgment would be negative and embarrassing. There are some differences. In ICD-10 public speech in front of a mass is not considered a phobic situation, as it is in DSM-IV, because ICD-10 specifies that the fear of being judged must be related to a small group of people, and not to a crowd. Furthermore, the DSM-IV specifies that the disorder must represent a socio-economic burden for a patient, what means that it affects professional functioning, while the ICD-10 does not require it. These differences are being revised, because many people, who live according to the limitations of the disorder, have set their life and professional goals below their prospects, and they can seem to be relatively successful. ICD-10 emphasizes the importance of body symptoms (blushing, sweating, hand trembling, or urge for urination), while DSM-IV refers only to symptoms of anxiety that occur in panic attack. Generally, the criteria in ICD-10 are somewhat stricter. Wacker and associates found that using this classification the social anxiety disorder occurs significantly less often than it occurs using the DSM-III-R (6).

There are two main clinically recognizable subtypes of social anxiety disorder today: generalized and specific (discrete). Generalized subtype is characterized by a fear of a wide range of social situations, and specific (discrete) subtype by a fear of one or several specific social situations. The most common fear is the fear of public speaking (speech, lecture, TV performance etc.). Some authors (e.g. Westenberg) consider this form of fear, without other social fears, a particular subtype of social anxiety disorder (7). It is not clear if it is only a spectrum of the intensity of this particular disorder, or is there a substantial difference between these subtypes. So

far, it has been noticed that patients with generalized subtype, when compared to those with specific (discrete) subtypes, are more often single, the disorder occurs earlier, they are characterized by a fear of interpersonal interactions, and they have a higher rate of alcoholism and atypical depression. Furthermore, compared to specific (discrete) subtype, patients with generalized anxiety disorder are younger, less educated and with a little chance for employment.

Sometimes, it is difficult to distinguish social anxiety disorder from agoraphobia or panic attacks. In agoraphobia dominates a fear from people as a crowd, and in social anxiety disorder there is a fear from negative judgment by individuals in that crowd, i.e., the fear of a person's own behavior, which will be judged negatively. If there still is a doubt, the agoraphobia should be given an advantage.

Panic attacks are not every time conditioned by social situation, while in social anxiety disorder it is always the case. Since social anxiety disorder is chronic, and occurs, on an average, 20 years before it is diagnosed, there is a little chance for the disorder to cease spontaneously. Only one quarter of patients recover from it. The chances for recovery are higher congruently to higher education, and higher age of a patient at the inception of the disorder and if there are no secondary mental disorders. As social anxiety disorder usually occurs in adolescence, a period that is important for education and future career, the impairment of the quality of their life is more serious (8, 9, 10, 11).

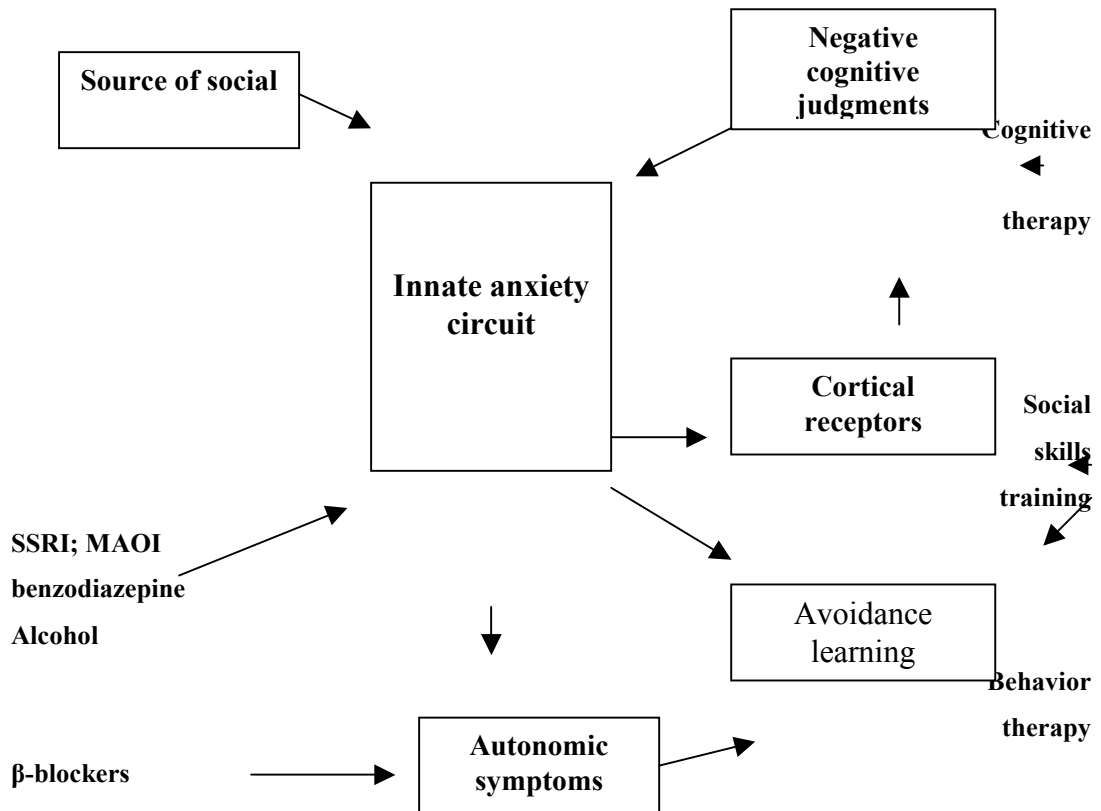
Etiology and development of social anxiety disorder

Social anxiety disorder occurs earlier than any other anxiety disorder, in the period of adolescence, and some of its characteristics can be noticed in children. Behavioral theories point to three key factors in the development of the disorder: direct fear conditioning, secondary fear conditioning (learning through observation), and verbal and nonverbal transfer of information about phobic social situations. In etiology of social anxiety disorder direct conditioning participates the most (50%). Analysis of particular social anxiety disorder subtypes show that etiological factors are represented differently. In the inception of specific subtype of the disorder the portion of directly conditioned fear is significant, while in generalized type of the disorder genetic factors play the major role. Family can influence the inception of social anxiety disorder in many ways: through direct conditioning, learning by observation, transferring information, and through biological hereditary factors. Sometimes it is difficult to distinguish the share of each factor in the inception of the disorder. For instance, some children are not in position to engage in social interactions or they are not in position to adopt every social skill they might need. Later, in adolescence, while becoming adult, it can be a significant constellation factor in the development of social anxiety disorder. Some parents support their children's avoidance behavior in dubious social situations instead of discussing them openly, what can induce fear in children. Family can influence positively and protectively if insists on social skills training in their children and helps them to manage potentially phobic situations. Behavioral inhibition in childhood precedes social anxiety disorder. If occurs early and if is conspicuous it is usually hereditary and is an early indication of generalized subtype. Nevertheless, it has to be mentioned, that not every patient with generalized subtype had exhibited behavioral inhibition during childhood. It is very

important to recognize behavioral inhibition, selective mutism and other early signs of social anxiety disorder in family and in school, because children never initiate their treatment due to their developmental cognitive limitations. Not recognized and inadequately treated social anxiety disorder in adolescence can lead to further psychiatric complications and can mask itself as depression, laziness, street fights, running away from home, vagrancy, theft, and substance dependence, and it is very hard to trace it afterwards (12).

Neurobiology of social anxiety disorder

Neurobiology of anxiety is complex and probably consists of interaction between several neuron pathways, which use several neurotransmitting systems. The knowledge gathered still is not complete, and schematic presentations that are used leave room for new hypotheses and discoveries. Concept of "innate anxiety circuit", although extremely simplified, is very useful to show the scheme of main components of social anxiety disorder and possible spots the available therapy methods could affect.



According to this model, persons with social anxiety disorder perceive social situations as threatening, what activates the innate anxiety circuit. The circuit provokes the inception of and reflexively feeds on negative cognitive judgments (to be embarrassed, to be incompetent). The circuit also activates the reaction of hypothalamic-pituitary-adrenal axis with characteristic cortisol response to stress (increased cortisol serum) and stimulates the autonomic system with consequential characteristic blushing, sweating and trembling. These body symptoms reflexively intensify the anxiety circuit by setting a positive reflexive loop, which worsens the condition further. When the unbearable level of anxiety and excitation of the autonomic nervous system is reached, the person is forced to look for the way out by learning how to avoid similar situations in future. Psychotherapeutic approaches, especially cognitive and behavior therapy and social skills training are confirmed to be very efficient in social anxiety disorder. They are directed to modifications of behavior and cognitive reactions in anxious conditions (13, 14).

β -blockers are not particularly efficient. Their positive effect is manifested only in weakened peripheral autonomic reactions, what can be used with the purpose to reduce the hand tremor and other signs of vegetative arousal in musicians, actors, etc. The efficient pharmacotherapeutics (benzodiazepines, irreversible and reversible MAOI and selective serotonin reuptake inhibitors – SSRI) act centrally, through innate anxiety circuit, which is in the middle of conceptual model of social anxiety disorder (15).

According to studies that use exogenous compounds to provoke anxiety, the sensitivity of chemoreceptors in social anxiety disorder runs between the normal and the sensitivity in panic attack. For instance, the reaction to lactate infusion in

patients with social anxiety disorder looks more like reaction in normal persons than reaction in patients with panic disorder, who react on it with increased anxiety (16). On the other hand, patients with social anxiety disorder are more sensitive to carbon dioxide than normal persons, and less sensitive than patients with panic disorder (17, 18). Intensified perspiration, blushing and tremor clearly show that the adrenergic system is involved in forming the symptoms of social anxiety disorder. This system seems to be less stable than in normal persons and includes increased stimulation of β -receptors on periphery. Therefore β -blockers can remove some peripheral effects of anxiety, but they can reduce the anxiety itself only as much as it is reflexively intensified by peripheral β -reactibility. Experimental studies show that persons with social anxiety disorder have a series of fine cardiovascular abnormalities that are characteristic for noradrenergic instability: their heart frequency more often becomes higher than normal while acting in public, and their blood pressure becomes lower than normal while getting up, and so on (19, 20). There is also plenty of evidence about the role of GABA-dysfunction in the inception and intensification of anxiety. Alcohol and benzodiazepines, stimulators of GABA neurotransmission, reduce social anxiety (21, 22).

There is few indirect evidence of dysfunction of dopaminergic system in persons with social anxiety disorder (23, 24). Finally, the efficiency of selective serotonin reuptake inhibitors in treatment of the disorder tells us that serotonin is important in its etiology. This is also supported by studies that point to oversensitiveness of 5HT_{2A}- receptors (24, 25) and anxiolytic-like effect of paroxetine in rats (26). It is not quite clear how the mechanism of selective serotonin reuptake inhibitors, which reduces anxiety in persons with social anxiety disorder, function, but postponed

effect of these medicaments suggests that it is a question either of postsynaptic desensitization or of intensification of presynaptic function. In fact, there are at least two serotonergic pathways involved in regulation of anxiety that have an opposite effect. For ascendant pathway that goes from nuclei raphe to amygdalae and frontal cortex, it is believed to reduce conditioned fear, and for the other pathway, from nuclei raphe to periacqueductal gray matter it is believed to inhibit unconditioned fear. In the first pathway serotonin is anxiogenic, and in another it is anxiolytic. The effect of selective serotonin reuptake inhibitors will depend on relative importance of each pathway in the etiology of social anxiety disorder (27).

Changes in cerebral function in persons with social anxiety disorder can be also presented by neuroimaging techniques. In healthy persons characteristic changes in blood flow through the brain can be recognized using positron emission tomography (PET) while provoking anxiety (28). It is interesting that only in persons with social anxiety disorder there is increased blood flow in the right dorsolateral prefrontal cortex and left parietal cortex, the areas important for planning affective responses and for awareness of the body posture (29).

Comorbidity in social anxiety disorder

Social anxiety disorder is a chronic and disabling disorder that often precedes other mental disorders, which dissemble it, and therefore clinicians have difficulties to recognize it (30). According to one large epidemiological study (31) 59% of examinees with social anxiety disorder had secondary simple phobia, 45% had agoraphobia, and 17% had major depression. Besides that, 19% were alcohol

dependent, and 13 % were drug dependent. In one French study of comorbidity in social anxiety disorder it was found that in 75% of cases it precedes depression at least a year (2). There are similar reports for agoraphobia (2) and eating disorders (32). Interesting observation is that comorbidity of depression and alcoholism in social anxiety disorder is more frequent in persons when the disorder occurs before 15 years of age (33). Suicidal risk is higher in social anxiety disorder with comorbidity than it is without it. Social phobia impairs the person's life, profession, family relationships, education and career often harder than heavy body impairment. Such persons rather infrequently get married; more frequently get divorced and more frequently stay unemployed than other persons.

Measurements of recovery from social anxiety disorder

Recovery from social anxiety disorder is a poorly defined concept. It is difficult to talk about full recovery after failing a career, missing the chances for better life, and being burdened with comorbidity. It is also difficult to evaluate how successful the treatment was, because the consequences of the disorder manifest in every sphere of the person's life. When evaluating recovery three criteria should be considered: objective – have the symptoms and avoiding behavior disappeared, i.e., are they reduced; adaptive – have the person obtained premorbid level of functioning that releases all the persons potentials; and subjective – does the person really feel well, i.e. does he or she consider his or her quality of life satisfactory. For measurement, suitable standardized scales are used. They can be divided into those that evaluate a person's clinical condition, disability and quality of life.

Some scales are generic, and others are specific. They are all based upon the questionnaire that is filled up either by clinician or by a patient. Generic scales for measurement of how serious the disorder is, are divided into those for global measurement (i.e. scale for Clinical Global Impressions – CGI) and those for symptomatic measurement (i.e. Hamilton Rating Scale for Anxiety - HAMA). Regarding specific scales one should mention a widely used Liebowitz Social Anxiety Scale – LSAS that consists of 24 items, 13 of which refer to public speaking situations, and 11 examine social interactions. Scales for measuring disabilities can also be generic (Global Assessment of Functioning, Sheehan Disability Scale) and specific (Liebowitz Self-Rated Disability Scale). Scales for evaluation of the quality of life are generic (WHO Quality of Life-100, Quality of Life Inventory and Short versions for clinicians with 36 and 12 items).

Therapeutic response to treatment with psychotropic drugs should be evaluated particularly carefully. Most often used generic scale for measurement of drug response is CGI, where significantly better and moderately better are considered to be satisfactory therapeutic response. For evaluation of the change of particular symptoms during the treatment, specific scale LSAS is used. Two measurement scales are particularly suitable to evaluate physiological symptoms: BSPS – Brief Social Phobia Scale and SPIN – Social Phobia Inventory. Since there is no one particular scale suitable to evaluate recovery, it is recommended to use several different scales every of which should evaluate a particular aspect of social anxiety disorder: symptoms, functioning and the quality of life (34, 35).

Psychotherapy of social anxiety disorder

In the treatment of social anxiety disorder efficient are only group behavioral and cognitive methods that are based on strategy of controlled exposure to feared situations. Psychodynamic oriented and other traditional psychotherapy methods are not efficient. There are two group cognitive behavioral psychotherapeutic techniques: Cognitive behavioral group therapy and social efficiency conditioning. They both involve exposure to a feared situation, but their purpose is different. Group cognitive behavioral therapy is directed to correction of cognitive mistakes, while social efficiency conditioning uses social skills training in order to make phobic situations more bearable. Group cognitive behavioral therapy has the significant advantage, because it is short, symptomatically directed intervention technique. It includes an educational component about the nature of anxiety, its various forms and etiological factors, and therapeutic technique training that also includes homework assignments. Exposure is essential in the treatment of this anxiety disorder. Therapy is usually carried out through 12 to 15 sessions of 2,5 hours each. Cognitive restructuring is the main component of this therapy technique. Social efficiency conditioning is directed to social skills training that in 28 sessions thematically train social skills in the period of 16 weeks, using purposeful exposure to specific situations that are phobic to patients in well-controlled conditions. The problem with these psychotherapeutic techniques is the lack of trained therapists who could carry them out, and therefore manuals for self-help with detailed directions of how to carry the therapy out at home are made (36).

Pharmacotherapy of social anxiety disorder

Main goals of pharmacotherapy in social anxiety disorder are:

- To relieve the patient of fear and cognitive distortions
- To reduce anticipating anxiety
- To reduce avoiding behavior
- To reduce autonomic and physiologic symptoms of arousal and anxiety
- To improve the patient's functioning and his or her quality of life.

In pharmacological treatment of social anxiety disorder following pharmacotherapeutics have been tested: irreversible and reversible MAO inhibitors, β -blockers, anxiolytics and selective serotonin reuptake inhibitors. Irreversible MAO inhibitors did not prove to be suitable for treatment of social anxiety disorder due to side-effects and a series of dietetic restrictions the patients have to follow during their application. Reversible selective MAO inhibitor – moclobemide, which have fewer side-effects and does not require strict dietetic restrictions proved to be more efficient in treatment of social anxiety disorder than placebo, in several studies, but results were not particularly impressive (37, 38).

Anxiolytic and quick effect of benzodiazepine are the cause of its extensive application in treatment of anxiety disorder. The effects are transient and it is recommended to prescribe them only as a temporary, additional therapy in acute phase of anxiety disorder. The effect of Alprazolam in one Placebo controlled study showed poor results Alprazolam : Placebo = 38% : 20%) (38, 39).

Better results have been achieved using clonazepam Clonazepam : Placebo = 78% : 20%). It is considered today that β -blockers, in spite of their ability to partially reduce body symptoms of anxiety, are not really effective in treatment of social

anxiety disorder (40). Selective serotonin reuptake inhibitors SSRIs are the newest group of antidepressants that are purposefully designed to act selectively and exclusively upon serotonergic system. Widespread serotonergic system in human brain and its various roles explain various clinical applications of this group of antidepressants. Therapeutic effect of SSRI will depend on relative importance of a damaged serotonergic pathway in the etiology of mental disorder. It is the same for social anxiety disorder where SSRI act in the way to recover the natural anxiolytic activity of serotonergic system (see Neurobiology of social anxiety disorder).

The most comprehensive database of treatment with selective serotonin reuptake inhibitors (SSRIs) refers to Paroxetine. After two small encouraging open studies (41, 42), wide multicentric and placebo controlled studies were undertaken. 850 persons with generalized anxiety disorder were included in three studies and were treated with paroxetine for 12 weeks in dosages of 20, 40, 50, and 60 mg daily. Positive effect of Paroxetine to clinical picture and functioning of patients in various areas of their lives is proved in all three studies (40, 43).

Information of other members of SSRI group in the treatment of social anxiety disorder comes from few small well-controlled open studies or case reports. Sertraline (44), Fluvoxamine (45), Fluoxetine (46), and Citalopram (47) also prove to be efficient in the treatment of social anxiety disorder.

Since social anxiety disorder is chronic, the prevention of the relapse is particularly important. Impressive are the results of a study by Stein and associates (42) in which, after 11 weeks of treatment with paroxetine, they classified patients with generalized social anxiety disorder to a paroxetine-group and a placebo-group. After

12 weeks in placebo-group was 62% of relapse, and in paroxetine-group was only 12%. The authors recommended pharmacotherapy application of three months at least. In another study, none of the patients that were on clonazepam during 12 months had relapsed, while among those who were put on placebo after 6 months there was 12% of relapse. The results advise that extended pharmacotherapy, after reducing the symptoms of social anxiety disorder, should continue up to a year. Indications for such extended pharmacotherapy are: persistence of significant symptoms, comorbidity, early inception of the disorder, more serious avoiding personality disorder, and information of relapses in the past. Since patients are most afraid of body symptoms of anxiety, which disclose their fear in phobic situations (blushing, trembling, sweating), particular attention should be directed to these symptoms when following-up the efficiency of the treatment. SSRIs are efficient in reducing these symptoms, and therefore there is no need to combine them with β -blockers. Bad therapeutic result can be seen from: early inception of social anxiety disorder, information of heredity, more serious clinic picture at the beginning of the treatment, comorbidity (especially alcoholism) and personality disorder (borderline, passive-dependant type). From all the above we can conclude that medicaments of choice for social anxiety disorder are first of all selective serotonin reuptake inhibitors and highly-potent anxiolytics. The first should be given an advantage, and the second should be applied occasionally in order to intensify anxiolytic effect in acute phase of the disorder (40).

Conclusion

Social anxiety disorder is the most frequent anxiety disorder (10-15%), which occurs in two subtypes – generalized and specific (discrete). In general practice it is still very poorly recognized. It is a disorder that occurs during adolescence and has significantly negative reflects to social life, working activity and the quality of life of an individual. Neurobiological basis of this disorder is still unexplored.

The disorder is frequently burdened with comorbidity with other anxiety disorders, depression and alcohol and drug dependence. In psychotherapeutic treatment of the disorder only cognitive-behavioral techniques are desirable, and the best results are achieved by combination of these techniques and pharmacotherapy. The medicaments of choice in treatment of social anxiety disorder are selective serotonin reuptake inhibitors. Anxiolitics should be used only as a supplementary in the acute phase. Treatment of social anxiety disorder should last at least 3 months up to one year.

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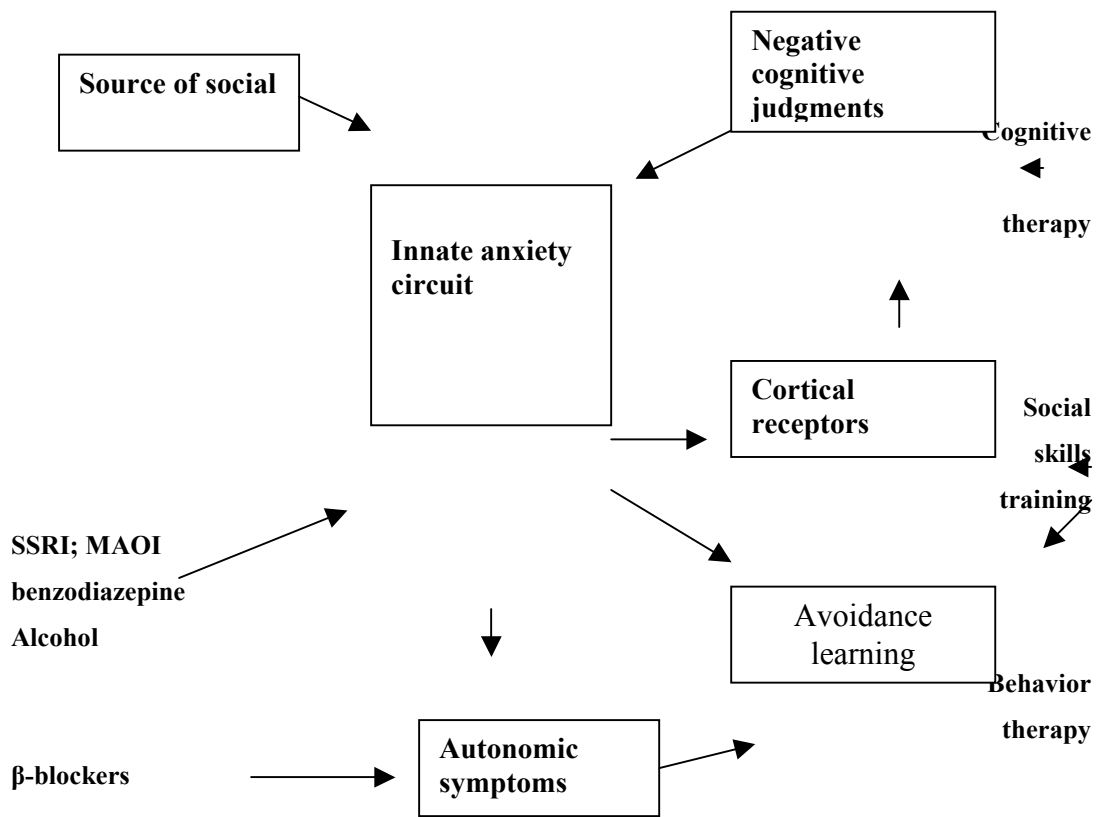
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