Treatment-Resistant Social Anxiety

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***Abstract*—Social anxiety, or generalized social phobia, can interfere with an individual's life on many levels, the professional and the personal. Social anxiety can also interfere with the autoregulative processes, which protect against various mental health conditions. The first lines of treatment are psychotherapy and a serotonergic antidepressant. However, in several cases even this combined approach may not be enough to effectively manage and cure social anxiety. Especially here a communication-oriented understanding and treatment approach can be very helpful.**

***Index Terms*—social anxiety disorder, generalized social phobia, generalized social phobia, treatment resistant, psychotherapy, medication, treatment, psychiatry**

I. Introduction

Social anxiety or generalized social phobia can be very debilitating to an individual. Since life depends on communication, and individuals need to communicate to be successful and attain happiness in life, anything that interferes with social interactions and meaningful communication can be a problem for the individual.

Communication

Social anxiety is an interesting disorder from a communication viewpoint because it

- interferes directly with external communication
- often precedes other mental health conditions

Social phobia is the primary disorder in comorbid conditions in close to three out of four patients. Re World Mental Health survey data indicate that social phobia has one of the earliest ages of onset amongst the mental disorders and yet is also one of the most undertreated anxiety disorders. Unfortunately, only roughly one third of patients afflicted with social anxiety seek help, about half of those who eventually seek help for one of the other anxiety disorders.

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Since many patients with social anxiety or social phobia are interested in social contacts and could otherwise be considered 'people persons', the term social anxiety seems more apt than social phobia.

A. Diagnosis

Social anxiety disorder (also known as 'social phobia') is an anxiety disorder in which there is a "marked and persistent fear of social or performance situations in which embarrassment may occur". In the major diagnostic manuals, the ICD-10 and the DSM-V, social anxiety is grouped with the anxiety disorder. This may also reflect a chief criticism of the diagnostic manuals, that they label bundles of symptoms rather than describing the etiology of a condition. This in turn means that individual conditions are associated based on their similarity in symptoms. From a manualized viewpoint social anxiety and generalized anxiety disorder are thus closely linked in how they are grouped. But even though they share several physiological symptoms this says little about the underlying psychological reasons that cause these symptoms, and which need to be the target of treatment to resolve the condition permanently. A more communication-oriented diagnostic system has been proposed by the author. (Haverkampf, 2010)

Social anxiety can be defined as nervousness in social situations. What is meant by 'social situations' is a situation where communication takes place among a number of people or in front of people. It is rarer that it affects people in one-on-one interactions. Some of it may be related to not having a sense of control or seeing the other person as judging and making this judgment personal and very important. Having a clearer sense of what is relevant and meaningful, a sense of purpose in interacting with oneself and others, usually facilitates communication.

Since communication on the inside and with the outside world is how humans get their needs met, implement their value and achieve their aspirations, it is not surprising that communication with others, as with oneself, is 'serious business'. This is complicated by the fact that internal and external communication are tightly linked. The success or failures in communicating with others reflects on the internal communication, while the successes and failures of the internal communication reflect on the external communication. It is thus not surprising that more than 90% of the population experience and suffer from social anxiety at some point in their lives. An

important step in therapy is to break down the concept of success and failure in communication by focusing on the true needs, values and aspirations of a patient, which is done using internal and external communication patterns. The beauty in the therapy of an anxiety to communicate is to use internal and external communication to create awareness for, reflect on and gain insight into communication patterns, which over time becomes increasingly natural and egosyntonic to the patient.

B. Symptoms

Individuals higher in social anxiety avert their gazes, show fewer facial expressions, and show difficulty with initiating and maintaining conversation. Trait social anxiety, the stable tendency to experience this nervousness, can be distinguished from state anxiety, the momentary response to a particular social stimulus. Half of the individuals with any social fears meet criteria for social anxiety disorder. The function of social anxiety is to increase arousal and attention to social interactions, inhibit unwanted social behavior, and motivate preparation for social situations such as performance situations.

C. Course

Social phobia has an early onset, with the median age of onset in the National Comorbidity Survey of 16 years. The most commonly reported fears relate to public speaking or speaking up in a meeting or a class.

The disorder is associated with significant disability. Patients with social phobia are more likely to utilize medical outpatient clinics, receive lower incomes, be less likely to earn college degrees, or attain managerial, technical, or professional occupations than people not suffering with social phobia. They are also more impaired in family relationships, romantic relationships, and desire to live, with over one in five having attempted suicide. The course of social phobia tends to be chronic, with a long duration of illness and low rates of recovery.

D. Comorbidity

Social phobia has a high degree of comorbidity with other psychiatric disorders. The odds ratio of having a second anxiety disorder is increased. Between one out of three to one out of five experience also suffer from a major depressive disorder, which often follows the social anxiety after twelve years. From a communication perspective, this overlap makes sense, as both depression and social anxiety are linked to changes in maladaptive and poorly working internal and external communication patterns.

One of four patients have also the diagnosis of an alcohol dependency, which should be viewed mostly as a form of self-medication. This also explains why the overwhelming majority, four out of patients develop the social anxiety before the alcohol abuse.

Some disorders associated with the social anxiety spectrum include anxiety disorders, mood disorders, autism, eating disorders, and substance use disorders. Many of these conditions are caused by interference with communication with oneself and others, and cause interference with communication processes. Often, it is possible to resolve the underlying issues of multiple conditions if one works at improving the patient's understanding and use of communication processes.

E. Cultural Influence

Cultures describes patterns of communication and how they relate to each other in an interactive social context. Recent data from the cross-sectional World Mental Health surveys shows great variation in 12-month prevalence in developing and developed countries. Rates are lowest in China and Japan (0.3% and 0.5%, respectively), range from 0.6% to 1.4% in European countries, and are somewhat higher in the Ukraine (1.5%), South Africa (1.9%), Mexico (1.9%), and Colombia (2.8%). Rates then jump to 5.1% in New Zealand and 6.8% in the US.

This data would need to be analyzed in greater detail, but it is obvious that a cultural setting plays a significant role. Of course, just because the rate is lower does not mean that there is less socially anxious behavior present in a population, but it does mean that the experienced suffering is probably lower, assuming that accessibility to mental health treatment, and acceptance of it, as well as similar systems of diagnosing a social anxiety disorder are comparable, a very steep assumption indeed.

II. Treatment

There are several treatment options for social anxiety, including medication, psychotherapy, and their combination. Although reviews of medications, psychological treatment, and combined treatments for social anxiety, and the development of clinical guidelines, has been numerous, there is little information of the underlying processes that lead to the symptoms.

III. Medication

For medications, selective serotonin reuptake inhibitors and dual serotonin-norepinephrine reuptake inhibitors are first-line choices based on their efficacy and tolerability profiles. However, other classes of drugs have shown effectiveness in treating some or most symptoms of anxiety, particularly on the somatic side, including also such non-psychiatric medication as beta blockers. Classes with demonstrated efficacy in social phobia include the benzodiazepines as a standby medication and antipsychotics, particularly the ones with a greater

serotonergic affinity as a frequent add on, or as a stand-alone, to manage more pronounced psychologically experienced anxiety. Alpha-2-delta ligands, such as pregabalin, represent another group, as do MAO inhibitors. However, it is questionable to what degree MAO inhibitors should still be used, given their potentially more adverse side effect profile, except in unique situations. The cost-benefit trade-off of MAO inhibitors is even higher when a patient is treated with medication combinations, such as in the case of comorbidity. Among the more experimental agents are neurokinin-1 antagonists or d-cycloserine, which are discussed further in another publication by the author.

Placebo-controlled RCT have been reported for several drug classes in social phobia. The greatest treatment response was apparently for the irreversible nonselective monoamine oxidase inhibitor, phenelzine, but there have been problems with sample sizes. However, this is usually not an option due the possible severe interactions with common food and other medication. Reversible selective inhibitors of monoamine oxidase A have a considerably smaller effectiveness in social anxiety.

The other three drug classes have demonstrated similar effectiveness for treatment response. Efficacy of the alpha-2 delta ligand pregabalin has only been reported at the 600 mg dose but not at lower doses; this higher dose is associated with high rates of dizziness and sedation. By default, this leaves SSRIs and the SNRI venlafaxine as first-line medication for the treatment of social anxiety. Since venlafaxine can in several people increase the anxiety even at first if not titrated up very slowly, the SSRIs are routinely the first point in the medication hierarchy.

A recent clinical guidance suggests a switching strategy, presumably based on data from the STAR*D studies, but this is not supported by clinical trial data.

1) Antidepressants

a) Selective Serotonin Reuptake Inhibitors (SSRIs)

This class of drugs is the most extensively tested in patients with social phobia, with several placebo-controlled acute treatment RCTs. The pooled OR for response to each selective serotonin reuptake inhibitor (SSRI) ranges between about two for fluoxetine to comfortably above three for paroxetine. In most studies, SSRIs showed separation from placebo by weeks four to six. Robust effects of the SSRIs in preventing relapse of social anxiety have also been shown in practically all studies that tested for it. This also bears out in clinical practice in the vast majority of cases. If a medication seems less effective, this is often due to external factors in the life of the patient, such as an increase in stressful situations in the workplace or in personal relationships, or to internal factors, such as the reactivation of an unresolved trauma process.

b) Serotonin and norepinephrine reuptake inhibitors

Venlafaxine is the only serotonin-norepinephrine reuptake inhibitor (SNRI) studied in RCT in patients with social phobia, but improvements in social phobia symptom ratings have also been shown in an open-label trial of the SNRI, duloxetine. All reported studies so far have shown significantly greater response rates for venlafaxine compared with placebo. At least one study has shown that over time there was no difference between a dose of 75 mg and one of 225 mg. However, in clinical practice often a difference can be seen in individual cases between 75 mg and 150 mg. The onset of response across all trials was evident at 4–6 weeks, although it could take three months for the full effect, similar to the SSRIs.

c) Monoamine oxidase inhibitors

The first placebo-controlled RCT in social social anxiety assessed phenelzine, an irreversible monoamine oxidase inhibitor. The rationale for using monoamine oxidase inhibitors was because social anxiety and atypical depression share the symptom of increased interpersonal sensitivity, and atypical depression is preferentially responsive to monoamine oxidase inhibitors.

Studies with irreversible MAO inhibitors consistently showed a significantly greater treatment response compared with placebo. Reversible selective inhibitors of monoamine oxidase A were developed with the intention of reducing safety concerns due to drug and food interactions with the original nonselective irreversible monoamine oxidase inhibitors. RCTs have been reported for brofaromine, a drug that was never submitted for regulatory approval, and moclobemide, which has been approved in many countries. The effectiveness of moclobemide seems relatively modest compared with other antidepressant drugs. In other words, there is rarely a reason to use the MAO inhibitors in the treatment of social anxiety. Given the range of medication from a diverse spectrum of groups available nowadays, there may not be a good reason for its use at all considering the profile of potential side effects of the MAO inhibitors.

d) Tricyclic Antidepressants

In clinical practice clomipramine may be useful in the treatment of social anxiety, but there is not enough empirical data to back that up.

e) Mirtazapine

Mirtazapine is an antagonist at 5HT2, 5HT3, and alpha2 adrenoceptors. There is no clear evidence for its effectiveness in social anxiety. Receptor antagonist antidepressants generally have not proven near as effective as the SSRIs and SNRIs.

Nefazodone, an antagonist at 5HT1a and 5TH2a receptors, did not separate from placebo in a single large clinical trial.

2) Antiepileptic drugs

The use of antiepileptic drugs in social phobia has been extensively reviewed recently. Only three antiepileptic drugs have been tested in RCT and show distinct differences in efficacy. Small open-label trials of valproate, topiramate, and tiagabine have also been reported, all of which showed some reductions in relevant social phobia rating scales.

Studies of levetiracetam do not point to much effectiveness in the treatment of social anxiety.

3) Alpha-2 delta ligands

Gabapentin and pregabalin are both ligands at the alpha-2 delta site on voltage-gated calcium channels. Functionally, both drugs reduce the release of a range of excitatory neurotransmitters through binding to this site. There are at least three positive RCT with alpha-2 delta ligands. The onset of anxiolytic effects is relatively rapid, occurring within the first week of treatment. The anxiolytic dose-response has only been formally assessed for pregabalin, and efficacy is only evident at the maximum dose (600 mg/day), but not at lower doses. This is in contrast with the effect of pregabalin in generalized anxiety disorder where the anxiolytic dose-response is seen at much lower doses (150 mg/day). There are no long-term treatment or relapse prevention data for alpha-2 delta ligands.

4) Benzodiazepines

In clinical practice, there appears to be widespread use of benzodiazepines alone or in combination with antidepressants for social phobia, but clinical evidence to support this use is relatively limited. There are three placebo-controlled RCT, one each for clonazepam, bromazepam, and alprazolam. All studies showed significantly greater improvement on a range of clinician-rating and self-rating scales compared with placebo. The mean doses used in these studies were generally modest (clonazepam 2.4 mg/day, bromazepam 21 mg/day, alprazolam 4.2 mg/day). The time course of response was only reported for the clonazepam study. Although there was a higher proportion of responders after one week of treatment (clonazepam 13.5%, placebo 0%), maximal response rates were noted after 6 weeks of treatment. Continuation of clonazepam treatment in treatment responders has been shown to decrease rates of relapse in social phobia compared with those switched to placebo.

Although the clinical practice of combining antidepressants and benzodiazepines appears to be common, it has been studied in only one small RCT. Combined paroxetine and clonazepam had a higher response rate (albeit not a statistically significant one) in an RCT in social phobia (79% versus 43%, P = 0.06) compared with paroxetine plus placebo.

5) Antipsychotics

The use of antipsychotics for the treatment of anxiety has been described by the author for anxiety disorders in general. (Haverkampf, 2012, 2013) In clinical practice, as a group they seem to be less helpful in social anxiety than in anxiety in general. If at all, the ones with the greater serotonergic affinity and the least sedation may be of some use in more severe cases of social anxiety.

6) Other agents

Negative RCT outcomes have been reported for buspirone, a serotonin 1A partial agonist, and for atenolol, a beta-adrenoceptor antagonist.

IV. Psychotherapy

There are several psychotherapeutic approaches that address the underlying issues in social anxiety at varying degrees of directness, efficiency and effectiveness. Communication-focused therapy (CFT) was developed by the author to work on the mechanism which is central and commonly affected in social anxiety, communication with oneself and with others. (Haverkampf, 2010)

From a communication perspective, most forms of psychotherapy work not necessarily because of the specific content they address or a skill they teach, but because a meaningful interactive relationship between two human beings affects their internal, and closely aligned with it, their external communication patterns. Several randomized trials of psychological treatments have been conducted.

Several studies have shown that various psychotherapeutic approaches are helpful in the treatment of social anxiety, if only because a psychotherapeutic setting puts the spotlight on the patient's external, and mostly also internal communication. Common problems of conventional psychotherapy studies are the plethora of unidentified variables that can play a significant role, such as the therapist's individual style, differences in manualization, concepts of what constitutes improvement, and the definition and treatment of the control groups, which may include waitlist control, psychological placebo, drug, drug-placebo, or treatment as usual (which may or may not include drugs). Most studies have used wait-list control which is the least stringent test of effectiveness. Recent meta-analyses of psychological treatments have found fairly large effect sizes for psychological treatments compared with wait-list controls with a Cohen's d of close to 0.90, but smaller effect sizes of close to 0.40 when compared with placebo or treatment as usual. But, as mentioned, there are good reasons to belief that communication mechanisms which underly human interactions in general can

be explored and practiced even better in a psychotherapeutic setting with its expectations and role assignments and the experience and training of the therapist. Since the school of psychotherapy may play a subordinate role, a focus on the communication patterns, and the change they can lead to in the communication dynamics, as practiced in communication-focused therapy (CFT) (Haverkampf, 2010), can be very helpful in the treatment social anxiety. This therapy, as developed by the author, works with awareness, reflection, insight and practice into the process, communication, which people feel anxious about/ Important is to realize that the more one knows about something, the safer one feels, and the sense of influence, efficacy and true confidence increases. Communication is not the exception but the originating point of this rule.

Most studies so far have investigated variants or components of cognitive behavior therapy (CBT), while this trend is shifting slowly, however, towards approaches with a longer (e.g. psychodynamic psychotherapy) and shorter history (mostly specialized therapies with a shorter track record). Some meta-analyses conducted subgroup analyses to determine whether inclusion of specific components of CBT, such as exposure, cognitive restructuring, relaxation, and social skills training makes a difference to treatment effectiveness. As can be expected from the foregoing discussion, significant differences in effectiveness as a function of inclusion versus non-inclusion of any of these treatment components where not found, nor did they find differences according to whether treatment was delivered individually or in group format. Maybe the only ineffective therapy is silence, the absence of communication, one could be led to believe.

In a randomized controlled trial, Stangier et al compared cognitive therapy with interpersonal psychotherapy. Both treatments were superior to wait-list control, but cognitive therapy was significantly more effective, a difference that was maintained at one-year follow-up. Still interpersonal therapy and mindfulness-based therapies may be useful add-ons or alternatives for individual patients or those who do not respond to treatment with CBT or another therapeutic approach.

Long-Term Effectiveness

A further important consideration is whether treatment effects endure. There is the risk that therapies which focus mostly on imparting strategies, or helping the patient develop those along defined manualized pathways, and educational aspects, which are main criticisms levelled against CBT, has been suspected to have a limited effect in the long-run, while approaches working with deeper dynamics, such as psychodynamic psychotherapy and communication-oriented psychotherapy, as developed by the author, have in clinical practice demonstrated longer remissions, most likely because the patient practically becomes his or her own therapist with the skills to identify patterns, gain insight and bring about the necessary changes. CBT on the other hand may require booster sessions, and there is a drop off in effectiveness after half a year to a year. However, this topic is still being debated, and so quite hotly in some quarters. Still, studies have shown that patients are probably more likely to be remission free and for longer than when stopping medication. A meta-analysis of nine RCTs of variants of CBT found significant effects at post-treatment (Cohen's d of 0.68 across all trials) that were maintained at follow-up, with no drop in effect size (0.76).

The availability of psychological treatments such as CBT is often limited by funding or therapist constraints, so recent RCT that have found Internet CBT to be equally effective as the therapist-delivered version are a promising development. More research is required to determine whether Internet therapy can be as effective as the therapist-delivered version for the full spectrum of social phobia severity and complexity. However, from a communication perspective it is to be expected that a limitation in communication channels (e.g. in decreasing richness from in person meetings to videoconference to telephone to chats / text messages, and so on). Software based therapy and phone apps may not be as limited in communication channels if they include video clips, for example, but the richness of feedback will always less than from another human being who shares the same neurobiological 'hardware' with the patient. This is also why good therapists who learn from experience and a genuine interest in people can be expected to be more effective than a manualized approach, which is often used in approaches like CBT. On the research side, however, this may necessitate a greater reliance on well-crafted case reports, which information technology can be an aid in linking and distilling information from them.

At least three studies have published follow-up data on outcomes after a treatment-free period. In all three trials, the psychological treatment showed greater maintenance of treatment gains or protection against relapse relative to the drug treatments.

A. Communication-Focused Therapy (CFT)

Communication-Focused Therapy (CFT) was developed by the author to focus more specifically on the communication process between patient and therapist. The central piece is that the sending and receiving of meaningful messages is at the heart of any change process. CBT, psychodynamic psychotherapy and IPT help because they define a format in which communication processes take place that can bring about change. However, thy do not work directly with the communication processes. CFT attempts to do so. CFT has been described by the author for several mental health conditions.. (Haverkampf, 2010) A few points that are encountered routinely in patients suffering from social anxiety are listed below. On the specific tools and strategies, it is best to consult the growing literature on CFT.

1) A Vicious Cycle

Patients with social anxiety usually have a desire to communicate with other people and are interested in communication, but they often have a higher expectation of themselves to 'get it right'. Whether it is that they feel they have more to lose from a social interaction or they have an elevated definition of what social success needs to be or what constitutes a failure, not engaging in communication with others decreases one's communication skills and sense of success even further.

2) Autoregulation Fails

One of the reasons why often there is no self-correction is that communication is such a central, and powerful, element of living organisms. It is necessary for survival and thus lacks the constraints of other parts of life. If it does not work, the organism withdraws to avoid feeling worse. What should now take place is reflection and learning to make communication with oneself and others work. Unfortunately, for various reasons, this often does not happen.

3) Wishes, Needs, Aspirations, Values

Communication is only an instrument, but its purpose is to maintain and ensure the survival of the individual, where survival does not only cover basic biological needs, but also the survival of a person with a sense of self. Thereby, communication ensures the survival of communication.

Having a purpose for communicating with oneself can facilitate the communication process. If there is a sense of purpose, the individual usually has enough motivation to get in contact with oneself and others again. This, however, usually requires having a clearer sense of what is relevant and meaningful to oneself.

4) Projection

Projecting one's own thought into the other is a common mechanism which contributes to social anxiety. It means that one is, for example, critical of oneself and then sees this in the audience or other people. Everyone is than as critical of the own person as oneself. The brain is usually not good at tolerating the unknown, especially if the anxiety level is elevated anyhow. So, it develops theories about another's thinking, motivations, intentions and feelings. However, the information it has about people who are strangers is very limited, so the own patterns of thoughts and feelings are used to make up for the unknown. Unfortunately, this leads to a situation where one is essentially communicating with a mirror image of oneself. If one has good thoughts about oneself, other people will also have positive thoughts about oneself. If one is very critical of oneself, other people are seen as no less critical of oneself.

Projection usually becomes much less of a problem, once one realizes that one is engaging in projection. However, it does take practice to prevent oneself from automatically engaging in projection.

V. Medication versus psychological treatment

At least three studies have published follow-up data on outcomes after a treatment-free period. In all three trials, the psychological treatment showed greater maintenance of treatment gains or protection against relapse relative to the drug treatments.

All social phobia treatment guidelines recommend some combination of medication and psychological treatment for optimal management of patients with social phobia. Meta-analyses have supported this quite clearly, although significant advantages of combination therapies are only evident with some drug classes and from a fairly small number of studies.

There are relatively few trials incorporating direct comparisons of medication with psychological treatments in social anxiety. There seem to be no significant differences in effectiveness between SSRIs and psychological treatments. meta-analyses of four monoamine oxidase inhibitor trials suggest that these drugs may be superior to psychological treatments, but the results were not statistically significant.

Synergistics

The real power in combinations of medication and psychotherapy lie in the synergistic effects. It is a clinical truism that a good, friendly, empathic and open relationship between patient and therapist with meaningful interactions increases the compliance for medication. This does not mean that the therapist and the prescriber have to be the same person, as long as the therapist has a good understanding of medication, which every therapist should. On the other hand, without medication a good number of patients would never be able to take part in therapy at a deeper more rewarding level, or in some cases not even be able to attend consultations, particularly if there is a comorbidity with generalized anxiety or agoraphobia.

There are at least five studies that have assessed treatment response in direct comparisons of medication with combined medication-psychological treatments in social phobia (two SSRI studies, two monoamine oxidase inhibitor studies, and one benzodiazepine study). For response rates in the SSRI and monoamine oxidase inhibitor studies, there were nonsignificant trends in favor of combined medication-psychological treatments over medication alone. For the single benzodiazepine study, there was a statistically significant advantage in favor of combined treatment. It should be noted that all studies were relatively small in sample size and thus may not have been adequately powered statistically.

There are at least four studies that have assessed treatment response in direct comparisons of psychological treatment with combined medication-psychological treatments in social

phobia (two SSRI studies, two monoamine oxidase inhibitor studies). For the pooled response rate in the SSRI studies, there was a nonsignificant trend in favor of combined medication-psychological treatments over psychological treatment alone. For the pooled response rate in the monoamine oxidase inhibitor studies, there was a significant trend in favor of combined medication-psychological treatments over psychological treatment alone. It should be noted that all studies were relatively small in size and thus may not have been adequately powered statistically.

The effectiveness of combined treatments for social phobia highlights the problem that psychological treatments are not widely available in many countries, and social phobia is one of the most prevalent mental disorders, suggesting significant unmet need for a state-of-the-art effective treatment. This makes the emerging evidence of the efficacy of Internet-based CBT, at least for uncomplicated presentations, a potentially important new opportunity to maximize the availability of combined treatments. However, this will probably never replace the insight and communication tools available to an experienced therapist.

Clearly, more research is needed to provide clinicians with better guidance in making treatment decisions, especially in light of accumulating evidence that the longer patients are unsuccessfully treated, the worse their long-term prognosis tends to be. However, with the clinical experience and the study results we have so far, a lot can be done, particularly with a synergistic combination of psychotherapy and medication, which should be regarded as the minimum of an effective treatment for social anxiety disorder.

Disclosure of Conflicts of Interest

The author reports no conflicts of interest.

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