

Pharmacological and Non-Pharmacological Interventions for Persistent Auditory Hallucinations in Schizophrenia

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Abstract

Refractory auditory hallucinations warrant evidence-based pharmacological and non-pharmacological treatment strategies. The current psychotropic medications have only modest anti-hallucinatory effect and the efficacy of non-pharmacological therapies is not well established. While clozapine seems to have the maximum anti-hallucinatory effect, some patients remain super-refractory even to clozapine treatment. Thus, going forward research should focus on the discovery of a derivative of clozapine that is free from the haematological side-effects, as this could lead to remarkable advancements in the treatment of schizophrenia. Recent years have witnessed an interest in the development of various forms of non-pharmacological approaches to addressing this problem alongside pharmacotherapy. Pharmacotherapy alone may not be the answer to refractory auditory hallucinations and a greater spectrum of non-pharmacological therapies is clearly needed. In this work, different forms of non-pharmacological therapies are reviewed, including CBT, which has gained popularity as a psychological intervention and an efficacious form of voice therapy. Antipsychotics are also reviewed, revealing that, despite having only modest anti-hallucinatory properties, they are essential for reducing the psychic pain and correcting the underlying psychotic process.

Keywords: Schizophrenia, hallucinations, clozapine, voice therapies, rTMS

Schizophrenia sufferers feel like abstract entities with non-animated bodies, often experiencing auditory verbal hallucinations (AVH) due to morbid “objectification” of inner dialogue.¹ From the patient’s perspective, AVHs are a subjective-objective phenomenon. AVH is a non-consensual, dynamic and psychologically charged experience and the voices often echo significant emotions. Derogatory voices are common representations of unconscious self-hatred that cannot stand up to the external world’s logic. Thus, patients need help to incorporate it. Auditory hallucinations may be arising because of an interaction between biological predisposition, perceptual and cognitive factors. According to an integrated model of auditory hallucination (AHs) suggested by Waters et al,² AHs arise from an interaction between abnormal neural activation patterns that generate salient auditory signals and top-down mechanisms that include signal detection errors, executive and inhibition deficits, a tapestry of expectations and memories. Recently, neuro-quantologists have proposed that AVHs may be an objectification of parallel thinking/quantum thinking.³ Parallel thinking is a source for thought insertion. There may be different variables of AVHs. Experiencing AVH has serious impact on the quality of life of the affected individual, and is a significant factor in prevalence of suicides among schizophrenic patients.⁴

Incidence

One in four schizophrenia sufferers experiences persistent AVH.⁵ AVHs are experienced by approximately 53% of schizophrenia sufferers⁶ and are present in 28% of major affective disorders (Goodwin & Jamison, .⁷ Evidence indicates that each patient responds differently to the voices, according to his/her evaluation of them (Table 1), which influences the degree of interventions. Specific dimensions of AVHs can give hints to the future likelihood of treatment resistance. Although the percentages differ in various studies, it is assumed that about 30% of patients have command hallucinations and they are seen as the ultimate betrayal of the mind.⁸ Often, the content of such messages is negative; thus, commanding AVHs are more distressing than commenting ones. Schizophrenia predisposes them to a greater risk of suicides and homicides. Command hallucinations are more prevalent among forensic patients and contribute to their forensic status.

The multi-factorial polygenic model of schizophrenic disorders has received great support and signifies that genetic factors play a bigger role than environmental factors in familial transmission of these disorders. Relevant studies provide little support for the mechanism of single major locus inheritance. A mechanism involving two, three, or four loci cannot be ruled out even though there is no compelling support for such models.⁹ It has

also been proposed that a single gene may be even responsible for hallucinatory experiences¹⁰ implying that those who have not inherited such a gene may not experience auditory hallucinations, but still could experience other characteristic symptoms of schizophrenia. One may also hypothesise that an individual who has inherited such a “hallucinatory gene” but not all the schizophrenia genes could hear non-clinical voices without having other schizophrenic symptoms. It is also arguable that those who carry such a specific gene are more vulnerable to experience hallucinations when they abuse psychoactive substances and could get misdiagnosed as having schizophrenia, but hallucinations may cease to occur once they abstain from illicit drug abuse.

Table 1 Patients’ Response to AVH

1. Anxiety and panic feelings
2. Fear
3. Feelings of humiliation
4. Entrapment
5. Self harm thoughts
6. Harm to others
7. Avoidant or withdrawn
8. Shouting and swearing
9. Ritualistic behaviour
10. Substance or alcohol abuse
11. Resistance.
12. Amusements
13. Engagement and courting the voices
14. Appeasement

Measurements for Assessment

AVH is a subjective experience and is hard to measure objectively. Several rating scales are now available for an efficient evaluation of different aspects of voice activities. Some are general and a number of them are specifically designed. Using rating scales facilitates better engagement with patients and helps in reinforcing the message that patients and the distress they experience are carefully considered.

Beliefs About Voice Questions (BAVQ) is an assessment scale useful in measuring the key beliefs about the voices.¹¹ It is typically used in conjunction with the Cognitive Assessment Schedule (CAS).¹² Voice Compliance Scale (VCS) is an observer rated scale aimed exclusively at measuring the frequency of command hallucinations and the level of obedience or confrontation with each recognized command.¹³ Voice Power Differential Scale (VPD) is another measure that can be applied to rate the perceived relative power differential between the voice and voice experience.¹⁴ On the other hand, Omniscience Scale (OS) is intended to quantify the voice hearer’s beliefs about their voices’ knowledge regarding the bio data.¹⁵ Another measure presently in use is Risk of Acting on Commands Scale (RACS), designed to assess the level of risk of acting on commands and the amount of associated distress.¹⁶

The Bonn Scale (BSABS) is used for the assessment of basic symptoms,¹⁷ while the Schizophrenia Proneness Instrument (SPI-A)¹⁸ and the Examination of Anomalous Self Experience (EASE)¹⁹ are useful aids in identifying minimal changes in subjective experience and for longitudinal monitoring (Table 2). In the extensively used Positive and Negative Syndrome Scale (PANSS), the hallucination item is one of seven in the positive subscale, which also includes delusions, conceptual disorganization, excitement, grandiosity, suspiciousness, and hostility. Given such a great number of scales in use, there is an obvious risk that differential anti-hallucinatory efficacy among antipsychotic drugs may be obscured by means of sum scores for the whole sample in clinical trials.

Table 2 Measurement scales

Beliefs About Voice Questions (BAVQ)
Cognitive Assessment Schedule (CAS)
Voice co Voice Power Differential Scale (VPD)
Voice Compliance scale (VCS)
Voice Power Differential Scale (VPD)
Omniscience Scale (OS)
Risk of Acting on Commands Scale (RACS)
Bonn Scale (BSABS)
Schizophrenia Proneness Instrument (SPI-A)
Examination of Anomalous Self Experience (EASE)
Positive and Negative Syndrome Scale (PANSS)

Treatments

Although many forms of treatments aiming to eliminate AVH or improve quality of life are available, use of medication seems to be the most prevalent. Besides drug treatment, non-invasive physical treatments, such as TMS and different forms of psychological interventions, have recently evolved. Drug therapies are aimed at symptom eradication, whereas psychological therapies tend to foster healing, recovery and personal growth. Rather than being specifically anti-hallucinatory, typically, neuroleptics offer a generalised calming effect and patients are given some “breathing space” to work through their voices. Usage of non-pharmacological tools is needed in the long-term management of refractory cases. Presently, intervention strategies for AVH are based on different models of hallucinations, but regrettably no clear models have been established.

Pharmacotherapy

The current understanding of AVH and the neural mechanisms involved is limited, and knowledge on how CNS drugs, such as antipsychotics, influence the subjective experience and neurophysiology of hallucinations is inadequate. Consequently, using pharmacotherapy in the management of AVH remains very challenging.²⁰ Despite multiple trials of different combination and adjunctive therapies to an antipsychotic regime, AVH can remain drug resistant. It is also important to note that all antipsychotics are potentially anti-hallucinatory, even though these effects are usually modest. Moreover, given

that, even when medications are effective, concordance can be an issue, antipsychotics should be used prudently and weighed up against effectiveness and side effects (Table 3). There are no clear guidelines for the drug treatment of AVH and comparisons of the efficacy of antipsychotics for AVHs are few. Clinical drug trials very rarely focus on single symptom scores, such as hallucinations, and tend to report group mean changes of overall psychopathology, or at best the positive subscale scores.

Evidences show that AVHs persist in spite of treatment in 32% of chronic patients²¹ and 56% of acutely ill patients.²² Trifluoperazine was popular as an anti-hallucinatory drug before the advent of atypical antipsychotic drugs. Clozapine is currently favoured for intractable AVHs and is beneficial in 30–60% of unresponsive patients.

Antipsychotic co-treatment is an option for clozapine augmentation. Olanzapine and risperidone may be alternative drugs in first episode psychosis. However, it is being debated whether clozapine should be used in such cases.

Table 3 Drug Treatment

Choice of antipsychotics
Cautions and contraindications
Titration of dose
Switching antipsychotics
Assessment of side effects, EPS, TD, Haematological effects etc.
Measuring the beneficial effects
Assess worsening of symptoms
Compliance

Clozapine

Use of clozapine is suggested only after two other antipsychotics have been tried. It works better with continued usage and clinicians have to be patient in its upward titration. At six months, improvement in Global Assessment of Functioning score is significantly higher for clozapine in comparison to other antipsychotic drugs.²³ However, when prescribing clozapine, cautions and contraindications must be noted (Table 4).

While higher doses of clozapine may not have more anti-hallucinatory effect, they still carry the risk of inducing the potential side-effects of this highly efficacious drug (Table 5). The most dreaded haematological side-effects are usually manifested within six months. For that reason, during clozapine therapy, patient has to be closely monitored, bearing in mind its limitations in achieving the anti-hallucinatory effects. If higher doses do not have the desired effect, clozapine dose should be titrated downwards to a point of its maximum anti-hallucinatory effect in a particular patient. Such an endeavour can prevent the emergence of serious side-effects, resulting in a complete failure of the therapy. The dose can also be adjusted to a safer level in cases where the psychological interventions are found to be successful. Clozapine can be effective even in lower doses, such as 200 mg/day. Only in the presence of command

hallucinations, higher doses should be prescribed to patients whose other positive symptoms are well under control.

Prophylaxis with an antiepileptic drugs, such as lamotrigine or sodium valproate, or similar should be commenced before titrating the dose above 600 mg daily. Close monitoring and active treatment of metabolic dysregulation should be initiated concurrent with clozapine therapy. In clozapine therapy, weighing up safety and superior antipsychotic efficacy and educating the patients on “clozapine lifestyle” is immensely important, as it helps in treating refractory cases of AVH. Thirty percent of patients treated with clozapine may remain unresponsive and clinicians have to lower their expectations to the level of achievement without being cynical. Isolated cases of clozapine-induced joint visual and auditory hallucinations have been reported.²⁴ In spite of Clozaril treatment having the highest anti-hallucinatory effect, a good percentage of AVH sufferers remain symptomatic and are classed as super-refractory.⁸ According to Gonzales (2006),²⁵ 50% of patients receiving antipsychotics achieve full remission, while 25% hear voices occasionally and 25% are unresponsive.

Table 4 Cautions & Contraindications of Clozapine

1. Patients with myeloproliferative disorders, a history of toxic or idiosyncratic agranulocytosis or severe granulocytopenia (with the exception of granulocytopenia / agranulocytosis from previous chemotherapy)
2. Bone marrow disorders
3. Patients with active liver disease, progressive liver disease and hepatic failure.
4. Severe CNS depression or comatose state, severe renal and cardiac disease, uncontrolled epilepsy, circulatory collapse,
5. Alcoholic/toxic psychosis and previous hypersensitivity to clozapine.
6. Pregnancy and breast feeding

Table 5 Benefits and risks of Clozapine

Benefits
1. Lower risk of suicide
2. Superior anti-delusional and anti-hallucinatory effects in refractory cases
3. Lower risk of tardive dyskinesia and suppression of TD.
4. Improvement in cognition
5. Higher quality of life and better adherence
6. Decreased relapse
7. Sexual functions unaffected
Risks
1. Agranulocytosis
2. Metabolic syndrome
3. Myocardites
4. Chronic constipation and bowel complications
5. Increased risk of seizure
6. Hypersalivation
7. Abrupt withdrawal cause marked discontinuation symptoms.

Benzodiazepines are often abused by voice hearers aiming to reduce their anxiety. Such patients might benefit by the addition of antidepressant, as this could enhance their mental resources to cope with the voices, even though they have no

anti-hallucinatory effects per se. Mood stabilisers are sometimes used to augment the efficacy of antipsychotics without any clinical validation. Despite multiple trials of different adjuvant therapies to an antipsychotic regimen, there have been few promising results. Still, in practice, clinicians may get frustrated, as they struggle to provide symptomatic relief to the voice hearers at any cost. Recently allopurinol, an anti-gout agent has been used as an adjunctive therapy and based on three randomized controlled trials, the result has been encouraging.²⁶

Psychological Interventions

Persistent AVHs alone may not warrant pointless alteration of medication, as non-pharmacological interventions may achieve some control. When clinicians are not cognizant of non-pharmacological therapies, AVH patients that do not respond to antipsychotics alone may be mislabelled as having refractory AVH. In fact, they are only unresponsive to drug treatment, and could potentially respond to an integrated approach. Similarly, patients with treatment-refractory AVH are often over-diagnosed as suffering from hard to treat schizophrenia, even when other positive symptoms have been ameliorated.

There exists a false dichotomy between physical and psychological treatment approaches to AVH. In practice, both treatment modalities have to be modified in a personalised form. After all, psychiatry was originally known as psychological medicine. Presently, even though different forms of non-pharmacological interventions are available for drug-resistant AVH, some have questionable effects.^{27,28,29} (Table 6).

Table 6 Psychological Interventions

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| <ol style="list-style-type: none"> 1. Cognitive behavioural therapy (C.B.T.) 2. Acceptance and commitment therapy (ACT) 3. Competitive memory training (COMET) 4. Compassionate Mind Training therapy (CMT) 5. Hallucinations focussed integrative therapy (HIT) 6. Mindfulness-based therapy 7. Normalizing techniques 8. Enhanced supportive psychotherapy 9. Attention training technique. 10. Distraction techniques 11. Self help approaches |
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CBT therapists predicate that AVHs are a manifestation of the morbid objectification of inner dialogue (thinking in words), and accordingly verbalised thoughts are the raw material for AVHs. Verbal thinking differs from external speech in many respects and has several distinct features. CBT therapists believe that cognitive dysfunctions underlie AVH and they target them with cognitive remediation strategies. Those experiencing voices commonly think that they are caused by a powerful external agency, and are controlling and potentially harmful. Psychological factors, such as meta-cognitive biases, beliefs, and attributions concerning the origins and intent of voices, also play critical modulatory role in shaping the experience of AVH.

Teaching patients to recognize the source of the voices alone has yielded beneficial effects.

Specific techniques have been designed to modify the frequency of AVHs and restore a sense of control over them. Earlier methods involved behavioural approaches based upon addressing hypothesized antecedents and reinforcers of voices and explored a variety of specific interventions such as relaxation training, graded exposure to voice triggers, manipulation of environmental possibilities and even aversion therapy.³⁰ These behavioural techniques were eventually expanded on by the application of cognitive methods. The primary aim of psychological therapy is to change the belief that voices are omnipotent and uncontrollable and to suppress the associated attributes of false identity, wrong intentions, and urges to harm oneself and others. They encourage patients to challenge irrational interpretations and modify maladaptive behaviour, diverting attention from voices with distraction techniques (Table 7).

Reality testing and behavioural experiments are one form of CBT intervention, based on the view that behavioural changes can prompt cognitive changes. Attention switching can also be used to challenge the belief that hallucinations are uncontrollable. Command AVHs are more prevalent among the forensic population and are more distressing than the commenting ones. The risk of the sufferer acting on them is high when voices are perceived as omnipotent and uncontrollable. CBT has been proven beneficial in tackling command hallucinations. Lack of insight and formal thought disorder may not necessarily disqualify CBT for AVH; nonetheless, negative symptoms may pose a barrier to this form of psychological intervention. The current model of CBT for psychosis has been criticized, suggesting that it is simply an extension of general CBT concepts without taking into account the specificities of psychosis.³¹ Patients with higher intelligence, who have the ability to grasp abstract concepts, might gain greater benefits from CBT.³²

Table 7 Goals of CBT

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| <ol style="list-style-type: none"> 1. Change false beliefs about AVH . 2. Challenge irrational interpretations. 3. Modify maladaptive behaviour – e.g. fear of the voices or hiding from them. 4. Divert attention, using distraction techniques. 5. Build and maintain treatment strategies 6. Develop cognitive behavioural strategies 7. Develop newer understanding of hallucinatory experience 8. Address negative self-evaluation. |
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Combining psycho-education and supportive psychotherapy has been found to enhance the functioning and self-esteem of voice hearers, providing a therapeutic structure. In the increasingly popular self-help voice-hearing groups, the ethos of recovery is understanding, accepting and integrating the sufferer's turmoil. Acceptance and non-judgemental support of

people with similar experiences has helped many patients cope with the condition. In response, the number of books on AVH, aiming to educate the sufferers and carers, has grown considerably.

Newer Psychological Interventions

Attention Training Technique (ATT) focuses on negating psychological distress through cognitive and meta-cognitive modification.^{33,34} Patients focus on up to five neutral sounds, such as a dripping tap, before switching their attention between different sounds. They then practise listening to all the sounds simultaneously. After a few weeks, they focus on neutral sounds and then on the AVH. Once this process is mastered, they switch attention between voices and other sounds, before being asked to divide their attention among them. This exercise continues for several weeks, whereby the aim is to replace the self-regulatory process with new processing configurations.

Acceptance and commitment therapy (ACT) is aimed at achieving psychological flexibility. It incorporates mindfulness and acceptance, considering AVH as a private experience and asserting that patients experience distress only when they try to deafen the voices. By reducing struggle with voices and engagement with them, key responses such as arousal, attention and activation of brain areas are hypothesised to be reduced.³⁵ The ideas behind ACT are consistent with the emphasis on the recovery movement of finding a way to live a valued life despite the ongoing problems. To this effect, unique and effective coping strategies are offered, whereby patients are given the insights that parts of the self are behind the voices. Thus, accepting them means sending a loving message of compassion, acceptance and respect to oneself. Two randomised control studies have yielded promising results.^{36,37} ACT follows a set manualised structure, rather than relying upon the complex and lengthy process of belief modification: therapy can be much briefer and potentially practiced by a wider range of clinicians and cost effective.³⁸

There are verbal and non-verbal routes to emotions. As CBT uses the former in voice therapy, it is less effective when patients are negatively involved with the voices. On the other hand, Competitive Memory Training (COMET) uses the non-verbal route. Generally COMET sessions involve four stages.³⁹ A. identification of aspects of negative self-esteem reinforced by the voice; B. retrieval and re-living of memories associated with positive self-esteem; C. positive self-esteem is brought to compete with the content of the voices to weaken associations between voice content and negative self-valuation; and D. learning to disengage from the voices and to accept the voices as psychic phenomenon.

The significant past comes back to the conscious mind in AVH, as life experiences charged with emotion make a compelling impression on the brain. The observation that voices are knowledgeable about patients suggests that auditory

hallucinations are linked to memory. In other words, negative experiences from memories evoke emotions, which should be deactivated. Distancing and decentring techniques could help patients to interpret voices as false mental events. As a result, incompatible memories could become tools to modify the power of voices—they are deactivated by new learning. Thus, when voices torment hearers, telling them that they are failures, a competing memory of such success as passing a significant examination is introduced. Posture, facial expression, imagination, self-verbalisation and music are all procedures included in the COMET protocol.⁴⁰

Compassionate mind training (CMT) is used to encourage better resilience to unpleasant commenting voices. CMT involves practicing exercises which promote self-compassion and compassion towards others. It is targeted to activate brain systems involved in social and self-soothing that amend threat systems active when experiencing unfriendly voices.⁴¹

Mindfulness is paying attention in a particular way – on purpose, in the present moment and non-judgementally. Clinical literature cautions against use of meditation in psychosis, but the effectiveness of mindfulness-based approaches for people with psychosis has been demonstrated in controlled clinical settings.⁴² and in the community.⁴³ Abba et al.⁴⁴ argue that effectiveness of mindfulness is a three-stage process: a. Becoming knowledgeable and developing more awareness of psychotic experiences and observing the thoughts and emotions that follow them. B. Permitting psychosis to come and go without reacting in order to cultivate understanding that distress is produced by the meanings one attaches to thoughts and sensations. C. Becoming autonomous by accepting psychosis and the self by acknowledging that the sensations only form part of the experience, and are not a definition of the self.

Neuroimaging studies are beginning to explain the neural mechanisms of how mindfulness might be working clinically. Structural changes have been observed in the anterior cingulate cortex, which is an area of the brain associated with emotional regulation.⁴⁵ There is evidence to suggest that mindfulness practice is correlated to reduced brain activity in the default mode network.⁴⁶

Limited improvements with mono-therapy have prompted the development of multi-modular approaches. Hallucination-focused Integrative Therapy (HIT) is geared towards integrating CBT with neuroleptics, coping strategies, psycho-education, motivational intervention, rehabilitation and family treatment.⁴⁷ Extant studies indicate that integrated treatment is more effective than TAU (treatment as usual).

The continuum model of psychosis and ordinary mental events has incited the development of normalisation of the voice hearing experience.⁴⁸ Most psychiatric symptoms occur in normal people—just as breathlessness and palpitations occur while exercising—but are potential clinical symptoms. It is the

frequency and duration that determine the borderline. According to the cognitive model, an internal mental event receives external attribution. Through normalisation, the external attribution can be reversed.

Although drug treatment may be the most practical way of managing AVH, refractory cases pose formidable challenges and it must be emphasized that psychological treatments are not counterproductive if applied skilfully. Clinicians who espouse the view that psychosis is a medical condition dismiss the usefulness of psychological interventions. The counter argument would be that a patient with a medical condition, such as stroke, benefits from physiotherapy, occupational therapy and psychological approaches.⁴⁹

Repetitive Trans-cranial Magnetic Stimulation

There are several ongoing trials in which the aim is to treat refractory AVH (Table 4). Repetitive transcranial magnetic stimulation (rTMS) is thought to alter neural activity over language cortical areas. Several studies on rTMS have shown improvement in the frequency and severity of AVHs, albeit without offering any strong conclusive evidence for its efficacy.⁵⁰ Moderate rates of AVH attenuation following rTMS have been noted in three meta analyses. Given that remarkable improvements in isolated cases have also been claimed, this suggests that rTMS may be appropriate mode of therapy for some patients.

Available data suggest that rTMS selectively alters neurobiological factors that determine the frequency of AVH. However, a recent meta-analysis indicated that the effect of rTMS may be short-lived (less than one month).⁵¹ Studies seem to indicate that rTMS may be effective in reducing the frequency of AVHs, with little effect on their other topographical aspects.^{50,52} Sham stimulation has also led to improvements in a number of AVH parameters. Compared to bilateral stimulation, rTMS of left temporo-parietal region appears more effective in reducing the AVH frequency.⁵³ To reduce the distress associated with AVH and help patients to cope with hallucinatory predilection, rTMS could be combined with CBT. The side-effect profile is much cleaner for this biological approach when compared to medications. Still, like any other anti-hallucinatory treatments, neuro-stimulation technique does not guarantee long-term elimination of AVH. Electroconvulsive therapy (ECT) is considered a last resort for treatment resistant psychosis. Although several studies showed clinical improvement, a specific reduction in hallucinations severity has never been demonstrated.

Avatar Therapy

Computer-assisted voice therapy is a budding form of computerised psychological treatment that is currently undergoing trials.²⁸ In this novel therapy, persecutory voices are directly depowered with the aid of a computerised dummy of the alleged persecutor through voice dialogue. Analytically-

oriented therapists can even converse with “voices” and such committed clinicians will find computerised voice therapy as another helpful tool. It is hard to ascertain whether the benefits of the avatar therapy were due to the specific technique involved or simply the increased attention and care, and Leff’s team acknowledged the limitations of their work.⁵⁴

Sound Therapy

Another important development in voice therapy is the use of tinnitus control instrument (TCI)—a form of sound therapy—in treating refractory AVH. Similar to AVH, subjective tinnitus is defined as the false perception of sound in the absence of acoustic stimuli. Even though their definitions are similar, the origin and underlying causes of these two conditions differ. Tinnitus is characterised by a simple sound—a monotone—and is non-verbal. In tinnitus, the brain is believed to interpret an internally generated electromagnetic signal as an acoustic sound or sounds.

Kaneko, Oda, and Goto²⁹ reported successful intervention in two cases of refractory AVH with sound therapy, using tinnitus control instrument (TCI) alongside antipsychotic medications. They posited that, in sound therapy, the auditory system is directly helping the limbic nervous system and the neuro-mechanism for AVH is sensitive to sound therapy.⁵⁵ They concluded that low-level auditory stimulation might be hindering the progression of voices and brain might be getting a breathing space to initiate self-healing process.

Future Directions

Hallucinogenic drugs, anti-hallucination medications and neuroimaging studies may lead to a better understanding of AVH. Animal models of hallucinations and pharmacogenetics might help to find more efficacious anti-hallucinatory drugs. AVHs themselves may have a genetic origin.¹⁰ Thus, not all patients that develop schizophrenia would experience AVHs. Such a finding might help shed more light on the genetics-linked mechanism and remedial measures of hallucinations in schizophrenia. Because the biological substrates facilitating drug effects on hallucinations remain largely unidentified, future studies with translational designs should address this important issue to find a more targeted drug treatment of psychosis.⁵⁶

If a derivative of clozapine without the haematological side-effects is formulated in the future, it might be an important milestone in the treatment of refractory AVHs and schizophrenia because clozapine has the most potent anti-hallucinatory effect. Such a novel drug could become the first line of treatment for schizophrenia, as it would address many of schizophrenic symptoms at their onset. This is crucial, as symptoms and habits become stronger and more resistant the more frequently they occur. Fatty acid amide derivatives of clozapine, such as DHA-clozapine, are found to have better pharmacological properties and enhanced safety. However, such claims are awaiting substantiation in clinical trials.⁵⁷ Thus, more

attention needs to be directed into this potentially rewarding research arena. It is, however, very likely that, even after a better pharmacological cure is found for AVHs, a few symptoms might linger on for long periods. With this view, efficient non-pharmacological remedies have to be designed to deal with such residual symptoms.

Discussion

Medications help reduce the psychic pain, and protect the dignity of patients, as well as prevent suicides and homicides. From the patient's perspective, the calming and relaxing effects of pharmacological therapies are a priority for relief from the distress due to AVH. Among the antipsychotics, clozapine has the maximum anti-hallucinatory effect and it is a shame that it cannot be used as a first line treatment choice. Treatment of AVH should be individualistic and clinicians should be prepared to apply several clinical and non-clinical approaches in concert to address them.

More research into the aetiology and mechanism of AVH is warranted in order to find effective treatment strategies. There is no shortage of theories about the mechanism of AVH, but there is no consensus among the investigators. It is unlikely that AVH is a pure neuro-chemical experience or a biological glitch, and this is where the currently available drug treatments fail. The distinction between primary and secondary symptoms was lost with the triumph of biological psychiatry in the last century. Thus, some authors presently claim that AVHs may even be a secondary symptom or a neuroquantological manifestation of an underlying biological disorder. We should not minimise the importance of eliminating symptoms when such symptoms are incapacitating, as in the case of hallucinatory experiences.

The present recovery model that emphasises and supports the patient's potential for recovery involving hope, supportive relationship, empowerment, social inclusion, coping skills and meaning cannot be achieved without the help of psychological interventions. In this respect, CBT is a useful tool in the rehabilitation of psychotic patients with residual AVH. Jauhar et al.⁵⁸ argued that the effectiveness of CBT in schizophrenia is influenced by failure to consider sources of bias. Consequently, the benefits are more apparent than real, prompting the question of whether CBT has been oversold.⁴⁹ The verdict of Maudsley debate on the issue has been that CBT has not been oversold, but rather has a great impact on symptom reduction and enhancing concordance and insight. Perhaps the most informative trial so far accomplished has been the work on cognitive therapy for command hallucinations, which has proven the benefit of specific model development, and which productively, combined measurement of process and a targeted outcome.⁵⁹

There is ample evidence suggesting that a combination of family and psychological interventions, alongside

pharmacotherapy, can be the most effective way of dealing with refractory AVH.⁶⁰ The inner dialogue hypothesis of AVH held by CBT therapists has its opponents.⁶¹ Patients respond to the voices they experience by utilising inner speech. Some observations with corresponding features weaken the inner-dialogue hypothesis. David and Lucas have demonstrated in a single case study that short-term maintenance of phonological representation (inner dialogue) may co-exist with AVHs – they are not synonymous experiences. The cost-effectiveness of psychological interventions is poorly studied, despite being highly relevant for policy decisions in healthcare.

Computerised voice therapy works better with technically minded, highly intelligent patients. In contrast, individuals of low to average intelligence may require a primarily behavioural approach, with limited efforts to understand concepts, such as automatic thinking and schema. Unlike sound therapy through music playing instruments (iPad, iPod, iPhone, etc.), TCI causes no disruption to daily functioning and can be used continuously. Computerised voice therapy and sound therapy warrant standardised case trials. When it comes to treating AVHs, optimizing compliance, reducing the burden of symptoms, and improving control, quality of life and social functioning should be the therapeutic goals.⁶² Neuroquantological views of AVHs⁶³ explain the limitations of pharmacotherapy and the usefulness of psychological interventions.

Competing Interests

None declared

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