Effects of SinuSonic on Psychological and Physical Well-Being

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Effect of the SinuSonic Device on Psychological and Physical Well-Being in Adults with Nasal/Sinus Congestion

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Brief background: Chronic nasal congestion impacts the functioning of the ventral vagal complex (VVC), which includes cranial nerves of the face and head (special visceral efferents), along with vagal regulation of the heart and lungs. Physiological compromise of the VVC due to a current or previous adverse experience may allow for worsening nasal congestion, which then has a circular impact back to poorer vagal regulation of the lungs.

This chronic cycle of congestion and poor vagal regulation can likewise impact mental health. Defensive symptoms/behaviors, such as anxiety and depression, are common emergent symptoms of a compromised VVC.

Purpose: The first aim of the study is to evaluate relationships between current/previous adverse events, degree of nasal congestion, perception of autonomic regulation and symptoms of anxiety and depression via self-report questionnaires.

The second aim of the study is to evaluate the effect of the SinuSonic on physical and psychological well-being in individuals with chronic nasal congestion. The SinuSonic is a self-applied nasal device designed to enhance physical well-being by reducing nasal congestion via simultaneous administration of acoustic vibration and gentle oscillating expiratory pressure. The vibration and expiratory pressure stimulate several cranial nerves that are included in the ventral vagal complex (VVC), including the cranial nerves of the face and head (special visceral efferents). According to the Polyvagal Theory (Porges, 1995, 1998, 2001, 2003, 2007), when the VVC is stimulated, the functioning of related cranial nerves and emergent behaviors should improve, supporting a calmer, more regulated nervous system, and improved mental health.

To evaluate the effects of the SinuSonic, self-report questionnaires will be administered (via RedCap) prior to beginning use of the SinuSonic, weekly during directed use of the SinuSonic (2 minutes per day, 2 times per day), and after 5 weeks of use of the SinuSonic. Weekly self-report questionnaires will include amount of SinuSonic usage and degree of nasal congestion. The final, 5-week questionnaires will include degree of nasal congestion, perception of autonomic regulation and symptoms of anxiety and depression.

As this is a feasibility/pilot study, data from the study will be used to estimate effect sizes and inform a larger, randomized trial on the effects of the SinuSonic on individuals with compromised autonomic regulation, if warranted by the results.

Background: The SinuSonic was developed as a non-phamaceutical device aimed to reduce nasal congestion via simultaneous administration of acoustic vibration and gentle oscillating expiratory pressure. Previous studies have demonstrated significant improvements in congestion and ease of breathing after immediate use of the device (Cairns & Bogan, 2019) and after twice daily use for 5-weeks (Soler et al., 2020). In this study, there was significant improvement in peak nasal inspiratory flow after only 2 weeks of use, and significant improvement in multiple self-report measures of congestion after 5 weeks of use. No adverse effects were reported. A review report by Schlosser, Salley and Soler likewise concluded that the device may improve pregnancy-related rhinitis, which may be particularly important for individuals who would prefer non-pharmacological interventions while pregnant or breastfeeding (https://sinusonic.com/blogs/learn/pregnancy-rhinitis.)

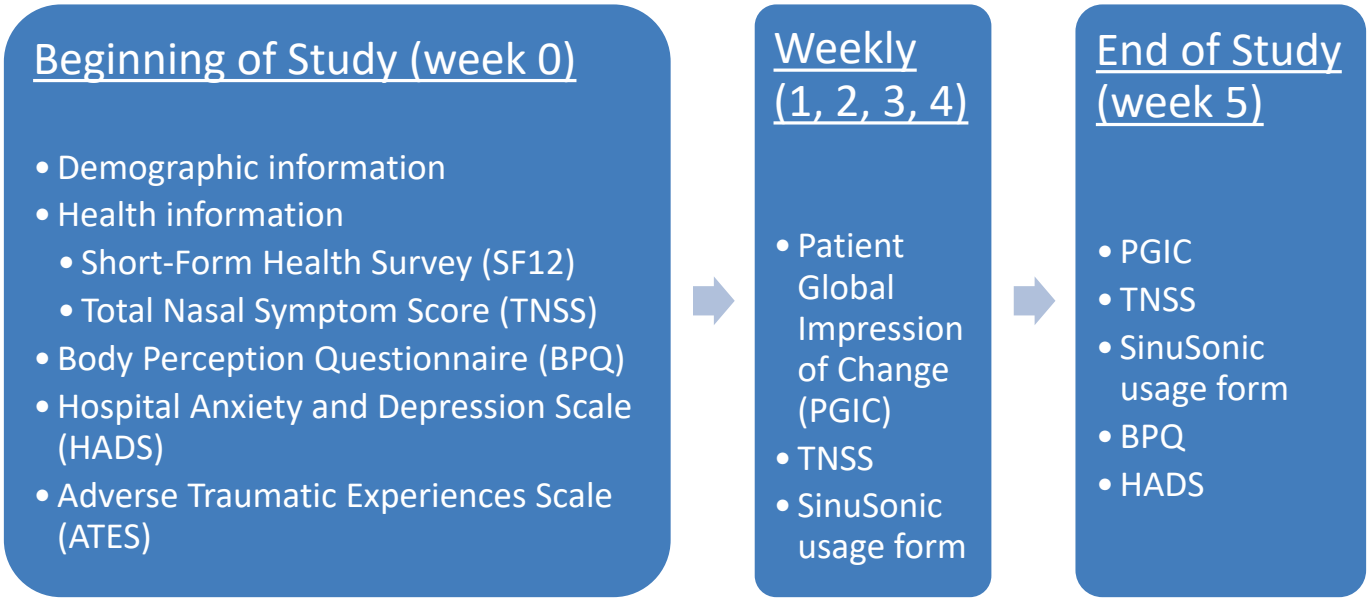
There are common clinical symptoms, such as anxiety and depression, that are frequently associated in individuals who feel unhealthy. The Polyvagal Theory (Porges, 1995, 1998, 2001, 2003, 2007) provides a model for which these psychological and physical symptoms may be viewed as the predictable consequences of a common neural substrate. This neural substrate involves the neural regulation of the heart and lungs, as well as neural regulation of the muscles of the face and head which function together as a Ventral Vagal Complex (VVC).

The VVC is based on the documented neuroanatomical and neurophysiological pathways between the brainstem areas that regulate the muscles of the face (via special visceral efferent pathways) and the heart and lungs (via the vagus). Features of the VVC may serve as a clinical checklist converging on symptoms of anxiety and depression as observed in several clinical disorders including autism (Bal et al., 2010; Patriquin et al., 2011; Porges et al., 2012; Van Hecke et al., 2009), Fragile-X-Syndrome (Heilman et al., 2011), selective mutism (Heilman et al., 2012), prematurity (Doussard-Roosevelt, et al., 1997), prenatal exposure to opiates and alcohol (Suess et al. 1997), PTSD (Sahar et al., 2001), perpetrators of domestic abuse (Umhau et al., 2002), Borderline Personality Disorder (Austin et al., 2007), behavioral regulation problems (Dale et al., 2011), and abuse and neglect (Dale et al., 2009). However, relating symptoms of anxiety and depression to an illness that impacts the functioning of the VVC (i.e., nasal congestion impacts the functioning of the vagus at the lungs) is a novel aspect of the current study.

Additionally, individuals who already have a compromised VVC due to adverse events (history or current), may also be at risk for the continued cycle of VVC complications (i.e., chronic congestion, anxiety and/or depression).

In summary, the function of the SinuSonic (i.e., reducing nasal congestion while improving vagal regulation of the lungs) align with the theoretical principles of the Polyvagal Theory. Thus, our proposed research will serve to determine whether the SinuSonic will have a significant impact on the reduction and management of physical and psychological symptoms (i.e, anxiety and depression), as they are described within the context of a dysregulated VVC.

Flowchart of Research Procedures:



Participants

50 adults (aged 18-99 years) with self-reported nasal congestion will be recruited for the study. Participants must be US residents.

Data Collection Procedures

Step 1: Recruit/Eligibility Screening

Individuals who make a purchase of the SinuSonic device will receive a recruitment flyer in the shipping box for their device, but only new users of the SinuSonic will be eligible to participate. The recruitment flyer will contain a QR code that users can scan to access the Eligibility Screening for the study in RedCap. Staff at SinuSonic has agreed to include the recruitment flyer when shipping packages.

The Eligibility Screening will consist of the following questions:

1) Are you between ages 18-99 years old? [YES TO QUALIFY]
2) Have you ever used the SinuSonic device? [NO TO QUALIFY]
3) Do you meet any of the conditions listed under the Safety and Warnings for use of the SinuSonic device? [NO TO QUALIFY]

   a) Current or history of breathing problems (i.e., asthma, chronic obstructive pulmonary disorder (COPD), chronic bronchitis, emphysema, pneumonia, pleural effusion, lung cancer, cancer of the throat or upper airway)

b) Current or history of circulatory problems (i.e., active nose bleed, heart arrhythmia, coronary artery disease, congestive heart failure, heart attack)

c) Other conditions, specified as brain tumor, moderate to severe ear pain, fever greater than 101 degrees

4) Have you experienced symptoms of nasal congestion that have persisted at least 2 weeks? [YES TO QUALIFY]
5) Is your current level of nasal congestion at 5 or higher? (VAS included here) [YES TO QUALIFY]

Step 2: Consent/Linkage File

When all eligibility criteria are met, individuals will be invited to access the Informed Consent document (also provided via RedCap) to read and e-sign. Phone number and email address for the researcher will be provided in the event of questions or request for clarification.

After receiving the e-signed informed consent, researchers will assign a SubjectID number so that the participant can use the SubjectID number when completing all questionnaire assessment sessions using RedCap. Researchers will maintain a database linking SubjectID and name on their password-protected computers that will not be accessible to anyone who is not affiliated with the research.

Step 3: Pre-SinuSonic assessment

Participants will be asked to complete this assessment, via RedCap, prior to beginning use of the SinuSonic. Researchers will provide participants with a link to the assessment (text or email), along with their unique SubjectID number to use. The following instruments will be programmed into RedCap for completion:

<u>Prior to SinuSonic Use (week 0):</u>

1) Demographic Information Form
2) SF12 to assess overall health ("how you feel and how well you are able to do your usual activities")
3) TNSS to assess current nasal symptoms
4) BPQ to reflect perception of autonomic regulation
5) HADS to assess anxiety and depression
6) ATES to assess history of trauma/adverse events

Step 4: SinuSonic Use / Weekly assessments

After completing the pre-SinuSonic assessment, researchers will inform participants to begin directed use of the SinuSonic (2 minutes per day, 2 times per day). Participants will be asked to confirm SinuSonic use on a weekly questionnaire. Additionally, participants will be asked to complete the following questionnaires approximately 5 minutes after final SinuSonic use for that week. The following instruments will be programmed into RedCap for completion:

Weekly, for 4 weeks (end of week 1, 2, 3, 4).

1) TNSS to assess current nasal symptoms
2) PGIC to reflect change in activity limitations, symptoms, emotions and overall quality of life

Step 5: Final research assessment

Participants will be asked to confirm use of the SinuSonic on a weekly questionnaire. Additionally, participants will be asked to complete the following questionnaires approximately 5 minutes after final SinuSonic use on the 5th consecutive week. The following instruments will be programmed into RedCap for completion:

End of Study (end of week 5).

1) TNSS to assess current nasal symptoms
2) PGIC to reflect change in activity limitations, symptoms, emotions and overall quality of life
3) BPQ to reflect perception of autonomic regulation
4) HADS to assess anxiety and depression

Description of Measures

Body Perception Questionnaire (BPQ) (Cabrera et al., 2018). The Body Perception Questionnaire (BPQ) is a self-report measure of body awareness and autonomic reactivity. Its items are based on the organization of the autonomic nervous system (ANS), a set of neural pathways connecting the brain and body. These pathways send information from the body about the status of organs and tissues (i.e., afferent projections). Some of these incoming signals form a basis for the subjective awareness of the body. The ANS also carries signals that control the functions of these organs and tissues (i.e., efferent projections). These signals can alter the functions of the body, depending on internal and external needs. Only the Autonomic Reactivity subscale will be distributed and used for the current study.

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). HADS is a fourteen-item scale with seven items each for anxiety and depression subscales. Scoring for each item ranges from zero to three. A subscale score >8 denotes anxiety or depression.

Short-Form Health Survey-12 (Ware et al., 1995). The SF-12 is a health-related quality-of-life questionnaire consisting of twelve questions that measure eight health domains to assess physical and mental health. Physical health-related domains include General Health (GH), Physical Functioning (PF), Role Physical (RP), and Body Pain (BP)

Total Nasal Symptom Score. The Total Nasal Symptom Score (TNSS) is the sum of scores for each of nasal congestion, sneezing, nasal itching, and rhinorrhea at each time point, using a four point scale (0–3), where 0 indicates no symptoms, a score of 1 for mild symptoms that are easily tolerated, 2 for awareness of symptoms which are bothersome but tolerable and 3 is reserved for severe symptoms that are hard to tolerate and interfere with daily activity. TNSS is calculated by adding the score for each of the symptoms to a total out of 12.

Adverse Traumatic Experiences Scale (ATES) (Kolacz et al., 2020). This measure asks about childhood adverse experiences, childhood maltreatment, other person maltreatment, life-threatening situations, sudden deaths of close ones, and personal health situations. Respondent-reported prior adverse events

of maltreatment, life-threatening situations, and sudden deaths of close ones are summed to create an adversity score (range: 0–19).

Patient Global Impression of Change (PGIC) (Hurst & Bolten (2004). The self-report measure Patient Global Impression of Change (PGIC) reflects a patient's belief about the efficacy of treatment. PGIC is a 7 point scale depicting a patient's rating of overall improvement. Patients rate their change as "very much improved," "much improved," "minimally improved," "no change," "minimally worse," "much worse," or "very much worse."

Data Analyses

Questionnaire data will be entered by participants into RedCap for researcher access. Researchers will export the data into SPSS for data analyses. All databases will be stored on password protected computers, accessible only to researchers affiliated with the study, and backed up on UNC servers.

As the current proposal is for a feasibility/pilot study, researchers will evaluate the following aims to determine whether a larger, randomized trial is warranted.

Aim 1: Examine associations between nasal congestion, autonomic functioning, adverse events, and mental health indices (depression, anxiety) at baseline. Pearson correlation analyses will be used to evaluate relationships among measures at each timepoint.

Aim 2: *(These would be the aims for a future, randomized clinical trial, with preliminary testing using data from the current feasibility/pilot study):* Evaluate the effect of the SinuSonic on users with chronic nasal congestion. We will focus on three constructs important to psychological and physical health and hypothesize that:

A) Nasal congestion will significantly improve when comparing baseline measures to follow-up measures at each week, and will maintain effects at 5 weeks. Repeated measures ANOVA will be used to evaluate mean change in outcome measures across time in PGIC and TNSS.

B) Autonomic functioning will significantly improve when comparing baseline measures to end of study. Repeated measures ANOVA will be used to evaluate mean change in BPQ across time.

C) Mental health indices (depression, anxiety) will significantly improve when comparing baseline measures to end of study. Repeated measures ANOVA will be used to evaluate mean change in HADS across time.

Aim 3: *(This would be an aim for a future, randomized clinical trial, with preliminary testing using data from the current feasibility/pilot study).* Evaluate the mediating effect of current/previous adverse experiences on outcome measures at 5 weeks, using regression models.

Aim 4: Calculate effect sizes for each outcome variable, which will be necessary to determine adequate sample size for a future clinical trial. G-Power software will be used to determine sample sizes based on the effect sizes of the current outcome measures.

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