The Neuros Behind NeuroZen:

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NEUROZEN

"Tapping into your body's natural reset button-the vagus nerve"

The Problem

Sjögren's disease is a debilitating condition that affects approximately 0.6% of adults in the UK, with a mean age of 50 years. Helper T cells perceive nuclear components that leak out of dead or damaged cells as antigens. These Helper T cells proliferate by mitosis to then activate B cells. This triggers the humoral response. Activated Helper T cells release cytokines that recruit more immune cells to the exocrine glands.

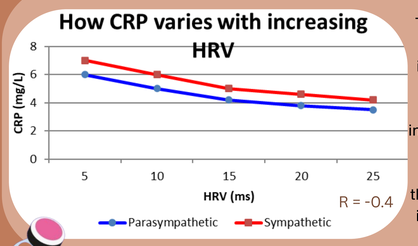
We chose Sjögren's syndrome as the focus of our project because it remains significantly under-recognised and frequently under-treated. It lacks visibility both within the medical community and among the general public, leading to delayed diagnoses and limited support for those affected. We aim to raise awareness of the challenges faced by individuals living with Sjögren's - particularly as 90% of sufferers are women, a demographic that has been historically and continues to be under-represented in clinical research and trials.

Earbuds offer an ideal solution because they are comfortable,non-invasive and are positioned close to the ABVN-enabling efficient stimulation.

Auricular Branch Of The Vagus Nerve

NZ buds connect to the ABVN (shown in yellow), which plays a vital role in reducing inflammation and fatigue. This is primarily due to the fact that the vagus nerve carries signals between the brain and body, regulating key functions like digestion, heart rate, immunity, and pain. As the main driver of the parasympathetic nervous system (PNS), it helps shift the body out of "fight or flight," promoting overall calmness, increasing HRV, and lowering stress. Electrical or sound stimulation of the ABVN activates both vagal and auditory pathways in the brain, enhancing neurological regulation and reducing fatigue. The auricular artery, shown in red, provides strong blood flow to the conchae, supporting clean PPG signals and accurate HRV detection.

Furthermore, stimulating the ABVN via the tragus activates the cholinergic anti-inflammatory pathway. This triggers a brainstem response that sends signals down the vagus nerve to peripheral organs like the spleen. In response, acetylcholine(neurotransmitter) is released and binds to α7 nicotinic acetylcholine receptors (α7nAChR) on immune cells such as macrophages. This interaction inhibits the production of pro-inflammatory cytokines — including TNF-α, IL-1β, and IL-6 — helping reduce systemic inflammation in conditions like Sjögren's syndrome.



This graph displays the relationship between HRV and C-Reactive Protein (CRP, an inflammatory biomarker). As HRV increases, CRP decreases, which indicates that the inflammation is being reduced due to the increased regulation from the nervous system. The parasympathetic nervous system is involved in the suppression of inflammation through the stimulation of the vagus nerve, so it has lower CRP levels than the sympathetic system

Our Proposal Vs Other Pharmaceutical Solutions

NeuroZen (ABVN Stimulation)

- Activates α7nAChR-mediated anti-inflammatory pathways via auricular branch vagus nerve stimulation
- Modulates immune function to reduce inflammation and fatigue without causing systemic immunosuppression or increasing infection risk.
- Non-invasive, at-home use; no regular dosing or medical oversight required
- Minimal side effects; suitable for long-term use
- An effective approach for controlling chronic inflammation with a low treatment burden and improved patient adherence.

Drug-Based Therapies (DMARDs & Corticosteroids)

- Disease-Modifying Anti-Rheumatic Drugs (DMARDs) exert systemic immunosuppression by targeting and inhibiting pro-inflammatory cytokine activity.
- Broad immunosuppression increases risk of infections and secondary diseases
- Oral or injectable; requires consistent dosing and routine medical monitoring
- Corticosteroids have strong anti-inflammatory effects,increasing ridk of liver toxicity, osteoporosis, immunosuppression, and systemic adverse effects
- Often challenging due to side effects and strict adherence requirements

Abbreviations:

PNS - Parasympathetic nervous system
NTS - Nucleus tractus solitarius
LRA - Linear Resonant Actuator
PPG - Photoplethysmogram
HRV - heart rate variability
tENS - transcutaneous electrical nerve stimulation
ABVN - Auricular branch of the Vagus Nerve
BCG-Ballistocardiography

Symptoms Of Sjogren's

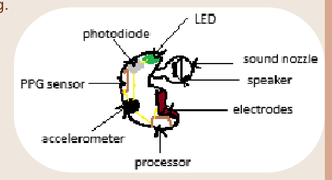
- Keratoconjunctivitis
- Xerostomia (dry mouth)
- Decreased saliva secretion
- Tooth decay
- Unintentional weight loss
- Raynaud's phenomenon
- Chronic cough
- Myalgia (muscle pain)
- Arthralgia (joint pain)
- Fever
- Fatigue
- Interstitial nephritis
- Mucosal atrophy
- Bilateral parotid enlargement

Our Proposal:

Our NeuroZen Buds (NZ Buds) deliver gentle, targeted electrical stimulation to the auricular branch of the vagus nerve, effectively reducing two of the most severe symptoms of Sjögren's Syndrome: chronic fatigue and persistent inflammation. By modulating the body's natural anti-inflammatory pathways ,NZ Buds offer a safe, user friendly solution that enhances daily life and overall well-being.

How does the NZ buds sensor work?

Our NeuroZen earbuds uses electrodes and PPG sensors (as seen in devices like Apple Watches) embedded in an earbud to non-invasively monitor HRV from the auricular branch of the vagus nerve, a key indicator of fatigue, stress, and inflammation in autoimmune conditions like Sjögren's syndrome. This branch is a main parasympathetic nerve influencing heart rate, and the earbud's closer proximity to it allows more direct, sensitive monitoring than wrist-based devices. Typically, HRV is extracted from ECG by measuring the time intervals between the R-peaks of successive heartbeats, which is considered the gold standard. However, the NZ buds use PPG technology, making it ideal for its compatibility with the earbuds, avoiding bulky, uncomfortable ECG setups.



The PPG system detects changes in blood volume by emitting green light through an LED, which penetrates the skin and reflects off blood vessels in the ear.

A photodiode detects the reflected light and converts it into electrical signals,

Converts optical signal into electrical signals

Electrical signals processed

Heart rate and inter-beat intervals (IBIs) are calculated, while HRV metrics such as RMSSD and SDNN are determined using the complementary NeuroZen app.

The app provide real-time insights into the user's autonomic state.

This diagram shows a cross sectional view of our earbud designed for health monitoring and neurostimulation.Key components like the PPG sensor and photodiode are positioned for HRV detection in the conchae,while the electrodes and processor are locared towards the tragus for targeted nerve stimulation

Since PPG signals are prone to distortion by motion artifacts, we have included a 3-axis accelerometer to detect and compensate for head or body movement using adaptive filtering and signal processing, ensuring accurate HRV readings during rest, relaxation, or guided sessions. The ear's stable position and proximity to the vagus nerve also reduce motion artefact compared to the wrist, resulting in higher signal fidelity.

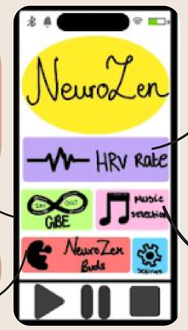
How will the electrical signals work?

- *The sensor will trigger a tENS electrode, which will send out the signals.*
- *The impulses pass through the skin and stimulate the afferent sensory fibres of the auricular branch. These fibres send signals toward the brain stem.*
- *The signals travel via the vagus nerve pathway to the NTS in the brainstem, influencing regions involved in autonomic control, mood, and pain processing.*

Each time an electrical signal is sent out, it will last for approximately 5 minutes; however, this duration can be adjusted via the app. The signal will also have a frequency of 12 Hz, which will therefore allow optimal binaural rhythmic stimulation as 12 Hz is associated with "calm wakefulness", which synchronises the brain with a relaxed state. This will reduce stress and anxiety, which will consequently lead to levels of fatigue, heart rate and systemic inflammation markers.

This is our model of NZ buds.
The design ensures contact with the auricular branch of the vagus nerve while housing an electrode module and sensor without protruding from the ear.

The Guided Breathing Exercise (GBE) complements stimulation by promoting nervous system regulation and boosting HRV through paced breathing. Regular practice can improve relaxation, support immune regulation, and complement the effects of NZ Buds.
Additionally the user will also be provided with the option to switch between the add on support systems(sound therapy/GBE) to suit their need.



The app tracks heart rate variability (HRV), a key biomarker of vagus nerve function and autonomic nervous system activity. If HRV drops, the user receives a notification and the NZ buds deliver electrical signals. Over time, the app builds a personalized HRV profile, enabling users to monitor progress and adjust stimulation intensity. This is especially important for autoimmune conditions like Sjögren's disease, where low HRV predominantly indicates inflammation or fatigue. Real-time tracking ensures targeted stimulation, helping regulate stress and immune responses

Sends important notifications—such as reminders to remove the earbuds—to minimise any potential health risks, including reducing prolonged exposure that could increase the chance of adverse effects.

Includes calming music and binaural beats to support relaxation and boost vagal activity-helpful for managing stress-related symptoms in Sjögren's syndrome.

Pros

- Real-time monitoring: Tracks HRV through the ear, providing immediate feedback via app and adaptive interventions.
- The stimulation of the vagus and the use of music to target the sensory pathways will reduce the heart rate by activating the PNS, which will reduce both inflammation and fatigue levels
- The earbuds are wireless, meaning there is free range movement, and they will also be very comfortable
- NeuroZen improves the quality of life for Sjögren's patients by 0.25 Quality-adjusted life years (QALYs) at a cost of £56 per device. This results in an Incremental Cost-Effectiveness Ratio (ICER) of £224 per QALY-well below the NHS threshold of £30,000, making it cost-effective.

Cons and future solutions

- HRV monitoring is disrupted by motion artifacts, so using a 3-axis accelerometer can reduce this. Future models could enhance reliability by complementing with BCG as found in 'ballisto buds,' or by incorporating an ECG method for the highest accuracy
- The ear buds need to be in contact with the tragus and be accurately positioned on the entirety of the conchae; therefore, for the best results, the NZ buds should be tailor-made to an individual's ear size. To combat this, we have included silicone pads on the buds to suit the needs of most, though this can be improved when patients go to their GPs and can have an accurate measure of their ear.
- The tENS has some restrictions, as not all people can use the earbuds. For example, those who have a pacemaker or have heart disease would not be able to use the device.

ETHICS

1. **Animal Testing:** The exposure of guinea pigs to electrical signals has the potential to cause pain, distress or hearing damage in them,however testing will be done under strict ethical guidelines, ensuring measures are in place to minimise discomfort.
2. **Environmental Impact:** While current manufacturing involves energy-intensive processes that releases toxins and contributes to the carbon footprint;by actively exploring biodegradable materials and improving recyclability ,long-term environmental impacts can be lessened.
3. **User Safety and EMF Exposure:**The wireless modules in our NeuroZen buds emit low-level, non-ionising RF radiation. While studies suggest cumulative exposure may cause slight tissue heating and inflammation in the ear and temporal lobe, strict safety limits minimise any risk during regular use.

Meeting Societal Standards

Feasibility

NZ Buds connect via Bluetooth and link to an app, giving users control while limiting access to prevent the stimulation from increasing to unsafe levels.

Acceptability

The NZ Buds are designed to be comfortable, easy to use, and discreet, making them acceptable to a wide range of users.

Affordability

With an estimated per-unit cost of approximately £56, the earbuds ear an accessible solution. Furthermore, collaborating with the NHS could significantly reduce the cost, enhancing wider availability .

Availability

The earbuds will first be available through GPs and hospitals to ensure safe use. Later, they can be ordered from a medical website with proper approval, not sold freely online, to avoid health risks

Pre-Clinical Testing

Stage 1 : 3-4 months
Check the proposal of the device and check all the elements within the earbuds to ensure that all the components will work synchronously.

Stage 2: 2-3 months
Carry out usability and software testing. Ensure the mobile app reliably connects to the earbuds via Bluetooth and can effectively control stimulation settings.

Stage 3: 4- 5 months
Before beginning the clinical trials, the earbuds need to be tested to test for cytotoxicity, irritation, sensitisation, and infection. Since guinea pigs have similar ears to humans and also have sensory nerves, this will allow researchers to observe any physiological or behavioural responses to stimulation. This, therefore, will allow us to identify any potential risks or effects of the earbuds.

Clinical Testing

Stage 1: 2 years
After getting the approval of the MHRA, begin the clinical testing. Firstly, test the earbuds on a group of 50 healthy volunteers. This will help us to understand any effects and the safety aspect of the earbuds. Any side effects should be recorded.

Stage 2: 2 years
Afterwards, use a random sample of 200 people who suffer from Sjögren's syndrome. In this stage, everyone should be monitored, and the stimulation vagus nerve system should be observed meticulously. Any symptoms should be recorded. Furthermore, goals and research should be set from this stage.

Stage 3: 4 years
More information about the safety and how the earbuds work will be noted. And now a larger sample of 1,000 people should be used. The efficacy of the earbuds should be watched and compared to already established treatments. Also, a placebo should be used in this stage to ensure reliable and non-biased results.

Stage 4:
In this stage, the earbuds will be tested with larger groups of people of different ages, sexes, ethnicities, and with different health conditions. Moreover, the earbuds can be used to test the treatment for other medical uses, different doses, or new combinations with other treatments. All of these analyses will help to see any long-term effects.

Once the device passes the clinical trials, it can be distributed to local GPs for use by patients suffering with Sjögren's syndrome