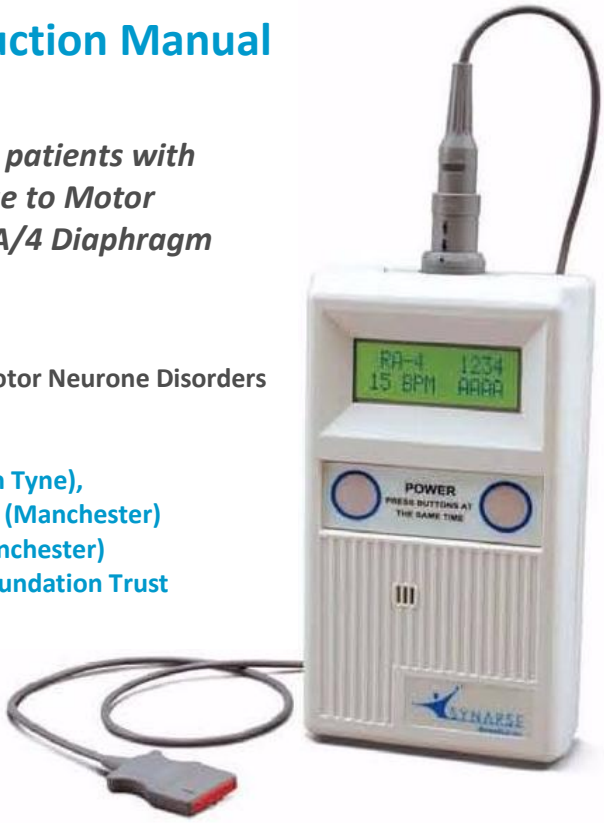
NeuRx Diaphragm Pacing System™

Patient/Caregiver Instruction Manual

PATIENT SECTION

A Randomised Controlled Trial in patients with Respiratory Muscle Weakness due to Motor Neurone Disease of the NeuRx RA/4 Diaphragm Pacing Trial (DiPALS)



MNDA Care and Research Centres for Motor Neurone Disorders
Royal Hallamshire Hospital (Sheffield)
John Radcliffe Hospital (Oxford)
Royal Victoria Infirmary (Newcastle upon Tyne),
University Hospital of South Manchester (Manchester)
Salford Royal NHS Foundation Trust (Manchester)
University Hospitals Birmingham NHS Foundation Trust (Birmingham)

V 2 24Jun11

Note: This document is controlled by study investigators at The University of Sheffield (Sheffield, UK). This document is not a Synapse Biomedical, Inc. controlled document. This document is a modified version of Synapse Biomedical document 77-0035 Revision E.

Key Contact Information

_____

Doctor:

_____

Nurse:

_____

Centre Name:

_____

Telephone:

_____

Fax :

_____

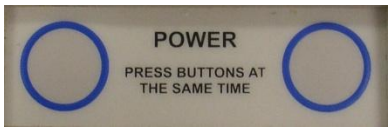
Address :

Table of Contents

LABEL SYMBOLS

Below is an explanation of the symbols used on this product and its packaging. Refer to the appropriate product to see symbols that apply.

CONTROL SWITCH SYMBOLS



CAUTION
ON/OFF switch buttons. Must be pressed simultaneously to activate and deactivate the Stimulator.

SYMBOL EXPLANATIONS

FOLLOW INSTRUCTIONS FOR USE

IEC 60601-1, Type BF Equipment

Conformite Europeene (European Conformity)
This symbol means that the device fully complies with Medical Device Directive 93/42/EEC.

IPX4 The device is protected from splashing water.

Output voltages may approach 50 volt D.C. during operation.

Serial Number

Moustapha Diop
Synapse Biomedical - Europe
156 Place des Aubépines
95680 Montlignon
France

WARNINGS

Use only under the direction of your study doctor. This device is electrically powered and may produce tissue damage or electrical hazard if improperly used. Do NOT attempt to open the Stimulator case; the device has NO patient-accessible controls.

This device should not be used if skin in the area is swollen, infected, or inflamed.
This device should be kept out of the reach of children.

PRECAUTIONS

Do not expose the pacing device to excessive moisture or severe mechanical shock. If display indicates system failure, pain is felt at the electrode site, or the device is exposed to moisture or shock, disconnect the cable and contact your study doctor or team.

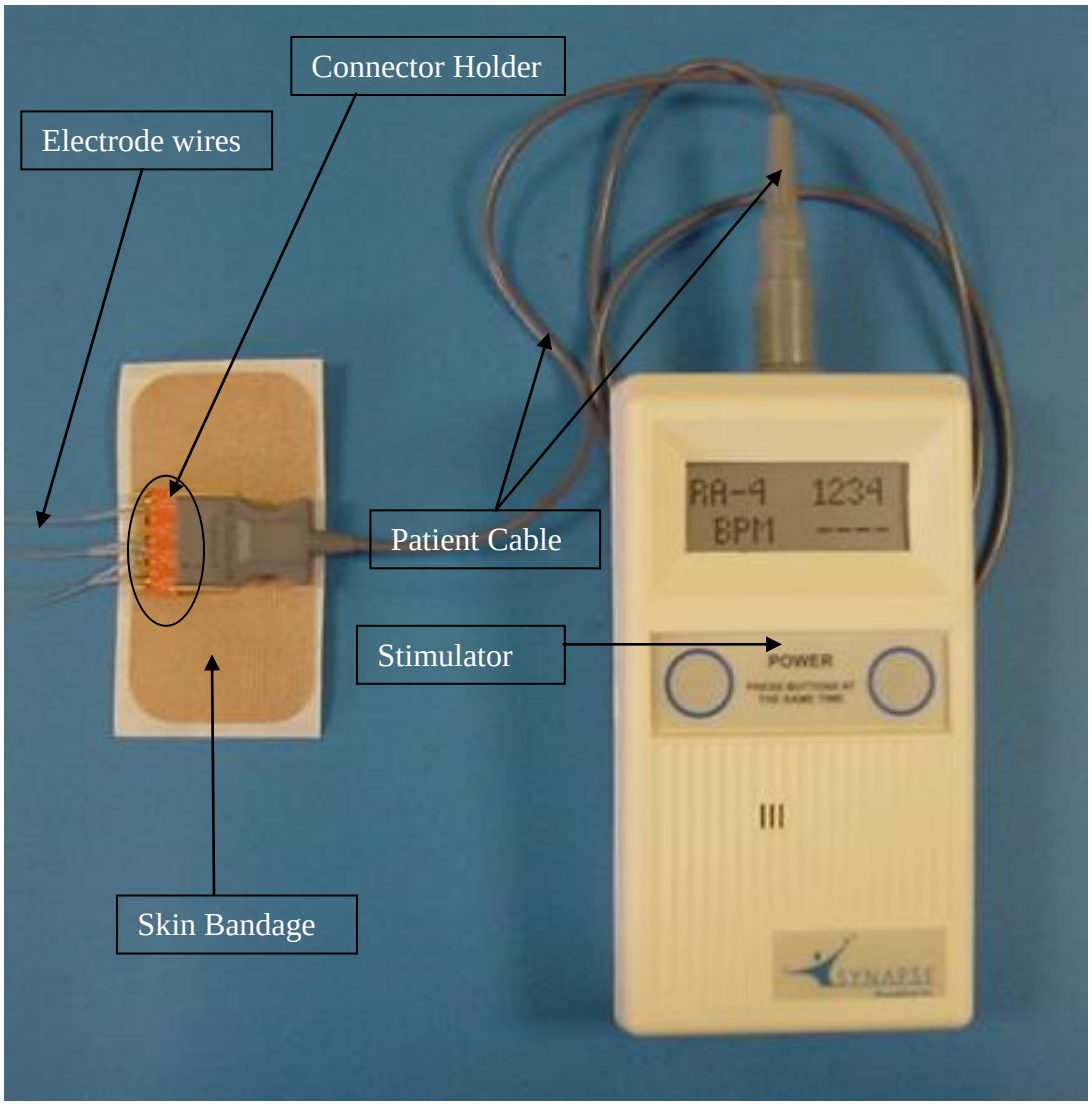
Some patients may experience skin irritation or hypersensitivity due to the electrical stimulation, the adhesive on the skin bandage, or the transparent dressing (Tegaderm™ and Op-Site™ are examples of transparent dressings) used over the gauze that covers the electrodes. Contact your study doctor or center if this occurs as irritation can usually be reduced by changing the stimulus parameters or removing the adhesive.

DEVICE DESCRIPTION

The NeuRx Diaphragm Pacing System™ is a system designed to help patients breathe by stimulation of their diaphragm muscles.

It is implanted using standard laparoscopic surgical techniques in an outpatient procedure.

The implanted intramuscular diaphragm electrodes are connected to the NeuRx™ RA/4 External Stimulator through the Patient Cable and the Connector Holder site.



The stimulator provides repetitive electrical stimulation to the implanted electrodes to cause the patient's diaphragm to contract and cause the patient to draw breath in a manner similar to natural breathing.

Your study doctor will program the Stimulator so that it produces the right stimulation patterns for you. If the stimulation makes you uncomfortable, tell your study doctor as he or she can adjust the Stimulator to reduce or eliminate the discomfort.

The user simply connects the device to the implanted electrodes and turns it on for use; no other controls are available or necessary for operation.

During use, the stimulator should be kept close to the patient's body to avoid pulling on the cable and electrodes.

The stimulator can be placed in a pocket of the patient's clothing, a small waist bag or simply placed on a table or other convenient location.

FUNCTIONAL FEATURES

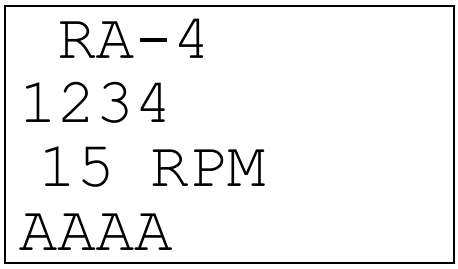
The cable should be securely inserted into the exit site connector and the top of the stimulator. The stimulator is programmed with parameter data that satisfies the patient's specific requirements.

To turn the stimulator ON: Depress the two buttons on the front of the stimulator simultaneously.

To turn the stimulator OFF: Depress the two buttons on the front of the stimulator simultaneously.

The buttons must be depressed simultaneously as a safety feature guarding against inadvertent activation.

The stimulator has a Liquid Crystal Display (LCD) that provides stimulator operational information.



The stimulator indicates the Breath-per-Minute (BPM) rate and when the individual electrodes are active.

During the breathing in phase, a letter ‘A’, ‘B’ or “C” is shown below each output number indicating that the stimulator is working well.

During the breathing out phase, a ‘-’character is shown below each output number indicating that the stimulator is not active.

In the event that an ‘X’ appears below an output number, then a problem exists and your study doctor should be contacted.

In the event that a ‘?’ appears below an output number, it should be immediately followed by a letter. This can occur normally when the pulse modulation parameter is set at a high value or when the pulse width parameter is less than 50 µsec. Your stimulator has been programmed with settings that have been established during your conditioning session. This is considered a normal event.

PATIENT INFORMATION

Motor Neuron Disease (MND, also known as amyotrophic lateral sclerosis, ALS) is a progressive neurodegenerative disease of unknown cause. One of the most important effects of progressive neuromuscular weakness in patients with MND is the effect on respiration. Although MND has no direct effect on the lung, it has devastating effects on all of the major respiratory muscle groups: upper airway muscles, expiratory muscles, and inspiratory muscles. Therefore, all patients with MND are at significant risk for respiratory complications.

Previous evidence suggests that peripheral muscle function can be preserved / improved in MND patients with a technique of electrical muscle stimulation.

The NeuRx DPS™ uses diaphragm pacing technology in an attempt to maintain respiratory muscle function in MND patients. If successful, at least two significant benefits may occur:

1. Life threatening respiratory muscle dysfunction may be delayed in paced patients.
2. Diaphragm pacing may be effective in ventilatory support of patients with MND either decreasing or obviating the need for negative or positive pressure mechanical ventilation

The NeuRx DPS™ connects to the diaphragm and delivers electrical current to stimulate the muscle contractions to preserve the diaphragm with the intended purpose of improving quality of life and slowing the progress to respiratory failure.

The diaphragm pacing system will provide stimulation to the diaphragm muscle to maintain its strength and potentially help with the breathing problems associated with MND.

The initial target for pacing sessions for MND patients is 5 times per day with each session lasting at least 30 minutes. Patients should build up to this target over the first month. In the second month patients should gradually lengthen the training sessions. When using 6-7 hours a day patients should then switch from pacing during the day to using the pacing device overnight whilst asleep. At this stage patients can additionally use the pacing device during the day if they

feel benefit but this is not essential. Patients should continue to use their NIV as advised by their study doctor.

CONDITIONING SESSIONS

The following describes the process of one conditioning session:

- Secretions should be cleared prior to conditioning and managed throughout the conditioning session.
- Connect patient cable to orange connector block and to the stimulator.
- Turn stimulator on.
- When conditioning session is over, turn the stimulator off.
- Disconnect patient cable from orange connector block.
- Document sessions on the conditioning log and include any complaints/discomforts noted in the comments section.

CONDITIONING WARNINGS

- The conditioning session should stop if you notice any change in heart rate or feeling of chest discomfort.

- The conditioning session should stop:

    - If signs of shortness of breath or any discomfort persists or worsens.
    - If management of secretions becomes difficult.

- You should not eat or drink while conditioning.

- External electrical stimulation should not be done in the chest area.

ALARMS

The stimulator initiates an audible alarm if it detects any of the following problems:

- If the connection from the cable to the box or the cable to the electrode wires becomes loose or disconnects
- A 10 seconds audible alarm will sound when the stimulator switches to the internal backup battery. The 10 second alarm repeats once every hour.
- A 20 second alarm will sound when the internal backup battery is low. The 20 second alarm repeats once every minute.

CARE OF CABLE

- The cable connects the exit site connector (wires) to the stimulator.
- Do not cut, kink or pull the cable
- Do not manipulate the metal pins in the end pieces of the cable
- Do not immerse in water
- Keep extra cables in a dry secure location
- When in use, the cable should fit securely into the exit site connector and the stimulator
- The length of the cable should be long enough to provide comfort and allow range of motion without pulling on the exit site connector
- Notify your study doctor or center if the cable gets cut, kinked, falls in water, loose connection to exit site connector or stimulator

CARE OF LEADS

- Do not pull on the wires coming through the skin
- Do not cut the wires
- Use extreme caution when shaving skin area around wire site

CARE OF EXIT SITES & CONNECTOR

- Keep the skin at the exit sites clean and dry
- Do not scratch skin at exit sites
- Clean the exit sites with alcohol wipe, allow alcohol to dry, place gauze dressing over the exit site. Be sure to cover all the wire with the dressing. Place a transparent dressing over the gauze. (Tegaderm™ and Op-Site™ are examples of transparent dressings)
- Change the dressings every 3 days or more often if the dressing becomes wet or otherwise soiled
- If the area becomes red, swollen, painful or drainage appears: notify your study doctor.
- Do not manipulate the metal pins in the connector
- The exit site connector should lie flat against the surface of the skin
- Observe that the electrode leads are properly positioned within the connector
- This connector will snap into a skin bandage (provided by the research team)
- Notify the research team if you there is a change in the appearance of the connector
- You should change the skin bandage weekly or if it becomes soiled

CLEANING OF COMPONENTS

- The surfaces of the Stimulator may be cleaned and disinfected with a less than 6% bleach solution or a less than 10% isopropanol solution. Typical cleaners such as glass or multi-surface spray cleaners are adequate.

- The surfaces of the Patient cables may be cleaned with a mild anti-bacterial hand soap solution.

LOW BATTERY

- If the stimulator displays “LOW BATTERY” then the battery needs replacement immediately. Contact your study doctor and/or team as they will need to replace the battery for you.

TROUBLESHOOTING

The following guide can be helpful in determining the source of problems with your DPS system:

Problem	Action
Pacing of the diaphragm stops	1. Check the connections of the electrode leads to the Connector Holder 2. Check the connection of the Patient Cable to the Connector Holder 3. Check the connection of the Patient Cable to the Stimulator
Patient Discomfort during pacing	Contact your study doctor. The Stimulator program may need adjustment
Bleeding, bruising, or infection of the electrode implantation site(s)	Contact your study doctor.
Patient feels pain at the electrode site	Disconnect the Stimulator first, then contact study doctor.
Skin irritation or hypersensitivity to stimulation	Contact study doctor.
Multiple "**X**"s appear on the Stimulator display	Disconnect the Patient Cable from the Stimulator and insert Test Plug. If problem persists then contact study doctor.
The Stimulator is exposed to substantial amount of water or fluid	Disconnect the Stimulator first, then contact Synapse Biomedical
Any alarm	Contact your study doctor

NeuRx Diaphragm Pacing System™

Patient/Caregiver Instruction Manual

HEALTHCARE PROFFESIONAL SECTION

A Randomised Controlled Trial in patients with Respiratory Muscle Weakness due to Motor Neurone Disease of the NeuRx RA/4

DiaphragmPacing Trial (DiPALS)

MNDA Care and Research Centres for Motor Neurone Disorders
Royal Hallamshire Hospital (Sheffield)
John Radcliffe Hospital (Oxford)
Royal Victoria Infirmary (Newcastle upon Tyne),
University Hospital of South Manchester (Manchester)
Salford Royal NHS Foundation Trust (Manchester)
University Hospitals Birmingham NHS Foundation Trust (Birmingham)

SYNAPSE
Biomedical Inc.

Table of Contents

WARNINGS

A potential safety hazard exists if there is a connection of the patient to a high-frequency surgical equipment and to the external stimulator simultaneously that may result in burns at the site of the stimulator electrodes and possible damage to the stimulator.

A potential safety hazard exists when operating in close proximity (for example 1m) to shortwave or microwave therapy equipment that may produce instability in the stimulator output.

The patient should avoid accidental contact between connected but unused applied parts (cable or leads) and other conductive parts including those connected to protective earth.

ELECTROMAGNETIC INTERFERENCE WARNING

The NeuRx™ RA/4 Stimulator needs special precautions regarding electromagnetic compatibility (EMC) and needs to be put into service according to the EMC information provided.

Portable and mobile RF communications equipment can affect the NeuRx™ RA/4 Stimulator.

Use of cables or accessories other than those specified may result in increased emissions or decreased immunity of the NeuRx™ RA/4 Stimulator.

FLAMMABILITY WARNING

The NeuRx™ RA/4 Stimulator is not intended to be used in an oxygen-enriched environment. The NeuRx™ RA/4 Stimulator must not be used near a flammable anesthetic mixture with air, oxygen or nitrous oxide.

PRECAUTIONS

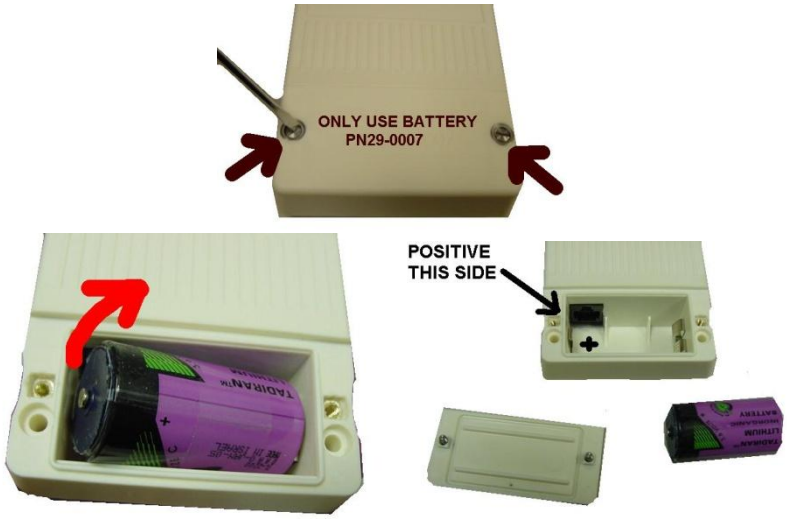
Precautions should be observed when there is a tendency to hemorrhage following acute trauma or fracture, following recent surgical procedures when muscle contraction may disrupt the healing process, or where sensory nerve damage is present.
Diathermy treatment and electro cauterization should be avoided in the area of the implanted electrodes. The stimulator should be disconnected during any types of electrical diagnostic treatment such as EMG or ECG.

BATTERY REPLACEMENT

(Instructions for Study Team)

Ensure that the Stimulator is turned OFF prior to battery replacement.

- ✓ Use only the battery specified on the Stimulator battery door. Do not use a standard alkaline battery in the Stimulator
- ✓ It is very important to install battery in the correct orientation
- ✓ It should be replaced every 500 hrs (3 weeks of full time pacing)
- ✓ The stimulator will initially display “REPLACE BATT” when your battery needs replaced.
- ✓ To change the battery, use the provided flat blade screwdriver to remove the battery cover located on the back bottom of the stimulator. Remove old battery and replace with new.
- ✓ Replace the battery cover and secure with mounting screws.
- ✓ Dispose of depleted batteries according to local regulations.



TROUBLESHOOTING

The following guide can be helpful in determining the source of problems with your DPS system:

Problem	Action
Pacing of the diaphragm stops	4. Check the connections of the electrode leads to the Connector Holder 5. Check the connection of the Patient Cable to the Connector Holder 6. Check the connection of the Patient Cable to the Stimulator
Patient is not receiving adequate ventilation	Disconnect the Stimulator and return the patient to a non invasive ventilation.
Patient Discomfort during pacing	Contact your study doctor. The Stimulator program may need adjustment
Bleeding, bruising, or infection of the electrode implantation site(s)	Contact your study doctor.
Patient feels pain at the electrode site	Disconnect the Stimulator first, then contact study doctor.
Skin irritation or hypersensitivity to stimulation	Contact study doctor.
Multiple "**X**"s appear on the Stimulator display	Disconnect the Patient Cable from the Stimulator and insert Test Plug. If problem persists then contact study doctor.
The Stimulator is exposed to substantial amount of water or fluid	Disconnect the Stimulator first, then contact Synapse Biomedical
A continuous audio alarm during the Inspiration Interval	1. Check the connections of the electrode leads to the Connector Holder 2. Check the connection of the Patient Cable to the Connector Holder 3. Check the connection of the Patient Cable to the Stimulator
The Stimulator beeps every hour	The Stimulator is running on its internal battery. Replace the main battery as described in this manual.
The Stimulator beeps every minute	The Stimulator is running on its internal battery and the internal battery is getting low. **Replace the main battery immediately** as described in this manual.

SERVICE

The RA/4 External Stimulator has no user serviceable parts and it is recommended that if the unit becomes inoperable it is returned to Synapse Biomedical, Inc for service.

REPLACEMENT PARTS

The following standard replacement parts may be ordered directly from Synapse Biomedical, Inc. as required.

ITEM	PART NUMBER	ORDER QUANTITY
Lithium Battery	29-0007	6
Patient Cable	22-0011	1
Connector Holder	22-0004	15

ACCESSORY

The following accessory may be ordered directly from Synapse Biomedical, Inc.

ITEM	PART NUMBER	ORDER QUANTITY
Screwdriver	29-0018	1

SPECIFICATION

Power Source	3.6-volt lithium battery
Battery Life	500 hours
Operating Temperature	+5 to +40 °C (+41 to +104 °F)
Storage Temperature	-6 to +60 °C (+20 to +140 °F)
Relative Humidity	10% to 85%
Pulse Waveform-type	Regulated-current biphasic
Pulse Amplitude	5mA to 25mA
Pulse Width	10use to 200usec
Pulse Period	20msec to 250msec
Inspiration Interval	0.8sec to 1.5sec
Inspiration Rate	8 to 18 Breaths per Minute

GLOSSARY

The following definitions are helpful in understanding the procedure and components of NeuRx Diaphragm Pacing System™.

Alcohol Wipe – individually packaged pad saturated with 70% Isopropyl Alcohol used to cleanse the skin's surface. For single use only.

Connector Holder – a bandage with a special plastic "shell" attached that is used to end of the Patient Cable

Diathermy – treatment procedure that uses high frequency energy waves to generate a deep heat of body tissues. Can be used as a treatment for pain relief

Electrode (or Percutaneous Electrode) – specially made thin wire, which is placed through the skin into the diaphragm and used to deliver electrical stimulation.

Electrode Connector – a plastic strip that the doctor connects one end of the Electrodes to, after implanting the other ends of the electrodes into the diaphragm

EMG – Electromyography is a method for measuring muscle activity via the electrical signals produced by muscles when they are stimulated.

ECG – Electrocardiogram is a recording of the electrical activity of the heart.

IEC – International Electrotechnical Commission (IEC) is an international standards organization dealing with electrical, electronic and related technologies.

Patient Cable – the covered wire that connects the Stimulator to the electrodes at the connector holder

Spasm – sudden involuntary or uncontrolled muscle tightening

Stimulator – a battery-operated controller that is programmed to generate a controlled amount of electrical stimulation

300 Artino Street
Oberlin, Ohio 44074
U.S.A.
www.synapsebiomedical.com

Tel :
888.767.3770
Fax : 440.774.2572

France +33 (0) 9 60 12 44 98
Other European Countries +33 (0) 1 64 95 23 99

CE
0086