Background and Rationale

Attentional set-shifting abilities are core features of several neuropsychiatric disorders. While in humans the verbal response allows for well-established tests, such as the Wisconsin Card Sorting, studying attentional set-shifting in mice is technically challenging, poor in reproducibility and time consuming (Scheggia et al., Nature Communications, 2018).

Dr. Scheggia and Dr. Papaleo's team invented a method called Operon (Scheggia et al. 2013), which:

◆ **Allows for multiple testing paradigms, whith the SAME MOUSE, across multiple dimensions.**

◆ **Is fully automated and software-controlled.**

◆ **Can be used with 2 (visual and tactile) or 3 (visual, tactile and olfactory) dimensions.**

At Ugo Basile, we developed a sophisticated machine including the necessary components to achieve the Operon tasks in a seamless way, through a fully assembled, software-driven machine.

What does it do: overview

The intrinsic limitations of current ID/ED attentional set-shift tests in rodents make them sub-optimal in terms of animal biases, time consuming and manually intensive aspects.

This represents an obstacle to the expansion of the science community who can run these highly relevant tests, in terms of human diseases, at the neocortical level. The Operon method aims at overcoming these limitations by a novel task, made of sequential subtasks, all run in the same mouse, by using a two-chambered device.

The beauty of the Operon procedure is that it allows to study through different tasks, all run sequentially in the same mouse, different cognitive functions, different neural circuits and neurotransmitters and all of the findings have strong human translational implications (e.g. for testing antipsychotic agents, cognitive dysfunctions relevant to psychiatric and neurodevelopmental disorders, such as Schizophrenia and many others).

In summary, with the Operon method and Ugo Basile new device, scientists can, in an automated and accurate way:

◆ **Dissect the function of different cortical regions.**

◆ **Prevent superstitious conditioning to unintended aspects of the stimuli.**

◆ **Perform IDS/EDS (Intra-Dimensional-Shift and Extra-Dimensional-Shift) stages, both serving as internal control and contributing to form the cognitive attentional test.**

NEW

1 Pellet dispenser

2 House light

3 Pellet receptacle

4 Led lights (programmable)

5 Nose poke and odor delivery/aspiration hole

6 Texture floor

Hundreds of combinations of stimuli across three dimensions (olfactory, visual, tactile)

The technology behind the Operon and the Outcome Measures

The instrument is composed of 2 compartments, divided by an automated sliding door, with an operant wall mounted on each side. The two compartments allow for the preparation of the subsequent task stimuli, while the mouse is still performing the current task, thus eliminating unwanted stimuli between the tasks.

Each operant wall includes double (left and right) automated tri-dimensional stimulators (visual, olfactory and texture), with 2 nose pokes and a pellet dispenser in the middle for the reward. 6 lights of 6 different colors are above each nose poke.

At Ugo Basile we have designed several unique components, specific for the Operon:

♦ **A Revolver System, lodging 6 out of 9 available different floor textures, providing automated tactile stimulation.**

♦ **An Odor Delivery System, managing 10 different odors, plus 2 channels for air cleaning.**

♦ **ANY-maze software, automatically managing all the Operon tools, following a pre-compiled protocol, and collecting the data.**

All is integrated, controlled and reported by the software to deliver the following outcome measures (and many more):

♦ **Number of trials to reach the criterion and number of errors.**

♦ **Time to reach criterion and to respond (latency).**

♦ **Mouse performance in a trial-by-trial base.**

Completely automated device: software-controlled inputs, data view and analysis

Multiple stimuli across 3 dimensions

Stimuli: 10 different odors 6 different lights 9 different textures

Features and Benefits

◆ Automated run of a sequence of multiple tests in the same mouse (SD, CD, CDRe, IDS, IDSRe, IDS2, IDSRe2, EDS, EDSRe), using multiple dimensions (tactile, visual and optionally olfactory); see Scheggia et al., Nature Communications, 2018

◆ 3 dimensions and up to 10 different stimuli for each dimension in the same apparatus

◆ Fully assembled device, ready to be used with the ANY-maze software, to design, perform experiment settings and analyze results

◆ Designed to be reliably combined with in vivo chemogenetics, optogenetics, electrophysiology, miniscopes, fiberphotometry

◆ Sensitive to changes in the different frontostriatal areas of the brain.
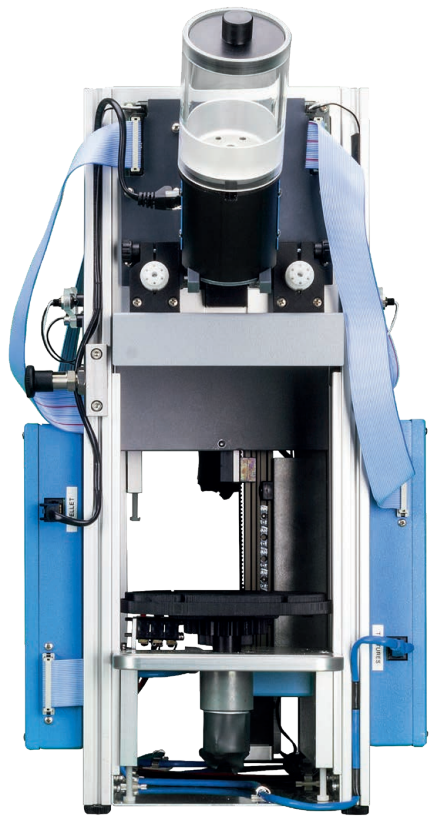
Specifications

Texture Revolver	6 tiles (2 neutral, velcro, plastic film, course sandpaper, fine sandpaper, smooth cardboard, ridged cardboard, honeycomb plastic, aluminum foil)
Stimulus lights	2 x 3mm, 6-color LEDs (WH/YE/BL/GN/RD/OG)
Nose-Pokes	2 x 12mm I.D. nose-pokes with aspiration
House Light	1 x LED lamp for each cage side (220lux, white)
Test/Data Management	via ANY-maze software (USB cable connection)
Power:	12VDC, 2A external power supply input 85-264 VAC, 50-60Hz

Physical	**Operon**	**Odor Delivery System**
Dimensions	30x60x55(h)cm	57x27x45(h)cm
Weight	15Kg	15Kg
Shipping Weight:	30Kg	30Kg
Packing:	50x66x62(h)cm	

Bibliography

◆ Diego Scheggia, Audrey Bebensee, Daniel R. Weinberger, and Francesco Papaleo: "TheUltimate Intra-/Extra-Dimensional Attentional Set-Shifting Task for Mice" Biological Psychiatry, Volume 75, Issue 8, Pages 660-670, 15 April 2014 https://doi.org/10.1016/j.biopsych.2013.05.021

◆ Diego Scheggia, Francesco Papaleo et alia: "Variations inDysbindin-1 are associated with cognitive response to antipsychotic drug treatment" Nature Communications 2018 Jun 11;9(1):2265. doi: https://doi.org/10.1038/s41467-018-04711-w Erratum in: Nature Communications. 2018 Aug 29;9(1):3560