Lt. Col. Simeone IZZO (MD, Psychiatrist)
Col. Gualberto ARDUINO (MD, Psychiatrist)

ITALIAN AIR FORCE
Aviation Medicine Institute
– Psychiatric Section –
ROME
STRESS RELATED SYNDROMES:

“Does the pharmacological treatment affect the performance?”

Performance
Clinical Syndromes
Antidepressant
Study-Methodology-Results

Discussion

Conclusions
What’s behind every human performance ???

.... especially like these ....
Always a human brain !!!

With its structural complexity
Sophisticated biological mechanisms
Brain activity is based on the **global and constant** communication between its own components *(through neurotransmitting systems)*

- in “normal” or “dysfunctional” conditions
Functional Complexity of CNS

- More than 50 chemical compounds acting as neurotransmitters
- Many types and subtypes of Receptor
- Billions connections/synapses
- Wide spectrum of effects
  \(\text{inhibition, activation, facilitation, modulation, promotion, repression}\)
Neurotransmitters & Receptors

- **SEROTONIN** (*modulation role*)
  - **Receptors**: seven types: 5HT 1-7 / several subtypes (A,B,C,D,E,F)

- **DOPAMINE** (*motivation, reward, cognitive, motor control*)
  - **Receptors**: two types: D1, D2 / subtype D1-D5- D2,D3,D4

- **NORADRENALINE** (*arousal, vigilance, learning, adaptive behaviours*)
  - **Receptors**: two types: Alfa 1,2- Beta 1,2,3

- **ACETILCHOLINE**
  - **Receptors**: Muscarinics M 1,2,3,4,5 – Nichotinics 1-7

- **GLUTAMMATE / ASPARATE** (*excitation, synaptic plasticity, learning and memory- Toxicity*)
  - **Receptors**: ionotrophics (NMDA, AMPA, Kainate), metabotrophics (mGluR1,2,3)

- **GABA** (*ubiquitary inhibiting system*)
  - **Receptors**: GABA a, b
A Ionotropo

B Recettore accoppiato a proteine G

C Recettore tirosina kinasi

D Recettore nucleare

(ad es., NMDA)

(+)

(ad es., D_1/D_3)

(ad es., TrkB)

Ca^{2+}

CAMP

PKA

CoMKII

Raf

MEK

ERK

RSK

Proteine

mRNA

Nucleo

CREB

c-Fos

Jun-D

CREM

ATF1

HRE
What do we expect from the brain performance???

Reliability !!!

....which means:

- vigilance
- attention
- situational awareness
- motivation
- endurance
- etc....
Is there something that could interfere ???
Sleeping disorders ... ?
lack of vigilance... ?
Impaired memory …?
INCREASING OF:

MOOD DISORDERS:
Depression, Dysthymia

ANXIETY DISORDERS:
Anxiety/Phobia
Panic Disorder
Obsessive Disorder
most common SYMPTOMS related to the clinical syndromes

- Anxiety
- Sadness
- Isolation
- Tiredness
- Irritability
- Introversion
- Helplessness
- Hopelessness
- Eating disorders
- Sexual disorders
- Sleeping disorders
- Lack of attention
- Memory impairment
Causes ???

Many factors !!!

Changes in

- Job profile
  *(uncertainty, risk, higher workload)*
- Rules
- Commercial policy
- Economics
- Family
- etc
Clinical target?

Recovery
Stability
Reliability

... for a safe performance!
CLINICAL GUIDELINES

ANTIDEPRESSANTS

use:

Selective Serotonin Reuptake Inhibitors
(S.S.R.I.s.)

Serotonin-Noradrenaline Reuptake Inhibitors
(S.N.R.I.s.)
Vie monoaminergiche cerebralì: 5HT
Vie monoaminergiche cerebrali: NA
Aim of the study

verify the impact of medium/long term treatment with antidepressant on mental performance
TWO GROUPS:

- **CONTROL (CTRL):**
  - 50 healthy subjects.
  - Male and Female
    - Mean age 41
  - Applicants suitable for the pilot licence medical certificate *(1st and 2nd class)*

- **CLINICAL (SS-N-RI):**
  - 50 subjects *taking* SSRIs or SNRIs for at least 6 months.
  - Male and Female
    - Mean age 42
  - Pilots
  - Flight Attendants
  - Flight Engineers
  - Air traffic controllers
neurocognitive testing battery

TACHISTOSCOPE:
perceptual speed, attention, vigilance
TREMOR TEST:
shaking intensity of the hand

neurocognitive testing battery
MENTAL EFFICIENCY:
short term/working memory, concentration

neurocognitive testing battery
neurocognitive testing battery

VISUAL RESPONSE TIME:
vigilance, reaction time
STRUCTURE of ANALYSIS:

**Multivariate ANalysis Of VAriance** for:

- comparable groups
- repeated measures
# RESULTS

- **MANOVA** - for groups

<table>
<thead>
<tr>
<th>Test</th>
<th>Control (CTRL)</th>
<th>Clinical (S.S/N R.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachistoscope</td>
<td>34.80</td>
<td>33.50</td>
</tr>
<tr>
<td>Number of correct answers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tremor</td>
<td>6.52</td>
<td>7.24</td>
</tr>
<tr>
<td>Number of significant shakes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental Efficiency</td>
<td>42.08</td>
<td>45.68</td>
</tr>
<tr>
<td>Number of correct answers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Response Time</td>
<td>201.08</td>
<td>214.90*</td>
</tr>
<tr>
<td>Speed average (mmsec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium variation (mmsec)</td>
<td>21.28</td>
<td>24.30</td>
</tr>
</tbody>
</table>
# RESULTS

**-MANOVA- for repeated measures**

*Time 1 – Time 2*

<table>
<thead>
<tr>
<th></th>
<th>CLINICAL (S.S/N R.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TACHISTOSCOPE</strong></td>
<td></td>
</tr>
<tr>
<td>N° correct answers</td>
<td>T1</td>
</tr>
<tr>
<td><strong>TREMOR</strong></td>
<td></td>
</tr>
<tr>
<td>N° of significant shakes</td>
<td>T1</td>
</tr>
<tr>
<td><strong>MENTAL EFFICIENCY</strong></td>
<td></td>
</tr>
<tr>
<td>N° correct answers</td>
<td>T1</td>
</tr>
<tr>
<td><strong>VISUAL RESPONSE TIME</strong></td>
<td></td>
</tr>
<tr>
<td>- speed average (mmsec)</td>
<td>T1</td>
</tr>
<tr>
<td>- medium variation (mmsec)</td>
<td>T1</td>
</tr>
</tbody>
</table>

(F “6,14” = 1.734  *p*= 0.185)

*any significant difference*

*stability of performance*
The only statistically significant difference is the higher visual response time in the “clinical” group:

- speed average: 201.08 vs 214.90 (mmsec)

No differences have been found for the other parameters evaluated

The performance is stable in the follow up
Common SIDE EFFECTS described for S-N RIs

Headache
Drowsiness
Dizziness
Slepplessness
Tiredness
Nervousness
Tremors
Difficulty concentrating
Appetite loss or increase
Weight loss or gain
Sexual disfunctions
Comparison:

**Side Effects**
- Headache
- Drowsiness
- Dizziness
- Sleplelessness
- Tiredness
- Nervousness
- Tremors
- Difficulty concentrating
- Appetite loss or increase
- Weight loss or gain
- Sexual dysfunctions

**Clinical Symptoms**
- Anxiety
- Sadness
- Isolation
- Irritability
- Tiredness
- Introversion
- Helplessness
- Hopelessness
- Eating disorders
- Sleeping disorders
- Sexual dysfunctions
- **Lack of attention**
- **Memory impairment**
What about other drugs/medications?

- ACE inhibitors
- Histamine- H2 Antagonists
- Proton Pump Inhibitors
- Calcium Channel Blockers
- Pain relievers-NSAIDs
- Bronchodilators
- Cough suppressants
- Decongestants
- Some “On-the-counter drugs”

Common side effects reported:

- Dizziness
- Headache
- Fainting
- Tremors
- Drowsiness
- Impaired vision
IMPAIRED in PERFORMANCE BALANCE

always present

clinical symptoms or dysfunctions

very little or rare, at start

side effects of medical treatment
THESE RESULTS SEEM TO CONFIRM OTHER FINDINGS AND ARE CONSISTENT WITH THE HYPOTHESIS THAT THE ANTIDEPRESSANT TREATMENT WITH SSRIs OR SNRIs IS:

- useful for the remission of the clinical syndromes
- useful for the prevention of somatic dysfunctions
- active on neurotrophic and neuroplastic brain process
- tolerated and safe, at “least but not less” than the syndromes themselves
F.A.A. (USA) has recently authorized use of SSRI in pilots:

- Paroxetine
- S-Citalopram
- Sertraline
- Fluoxetine

... with some prescriptions !!!
Conclusions

INCIDENCE OF PSYCHOLOGICAL DYSFUNCTIONS (mainly those related to stress) IS INCREASING, EVEN IN THE AIRCREW COMMUNITY

AN APPROPRIATE, STANDARDIZED AND ALLOWED PHARMACOLOGICAL TREATMENT PROTOCOL is ready to be introduced in the aviation medical rules (like other treatments)
Thank you!

Q U E S T I O N S  ???