



PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga



SISTEMA NAZIONALE DI ALLERTA PRECOCE
NATIONAL EARLY WARNING SYSTEM - N.E.W.S.

Report and Abstracts

International conference

NEW DRUGS 2014

Scientific and technical update
on New Psychoactive Substances

May 14th-15th, 2014

Universita' Cattolica del Sacro Cuore
Centro Congressi Europa - Auditorium

Rome

NSP project Alert 2013

In collaboration with



UNODC

United Nations Office on Drugs and Crime



unicri

United Nations
International Crime and Justice
Research Institute



European Monitoring Centre
for Drugs and Drug Addiction



Presentazione

Presentation



Elisabetta Simeoni

Dipartimento Politiche Antidroga / Department of Antidrug Policies

Presidenza del Consiglio dei Ministri / Presidency of the Council of Ministers

Negli ultimi anni si è assistito ad un fenomeno del tutto nuovo che ha rivoluzionato le tendenze giovanili, e non solo, rispetto all'uso di droghe. Alle sostanze tradizionali (cannabis, cocaina, eroina, ecc.) si sono aggiunte Nuove Sostanze Psicoattive di origine sintetica di cui ancora molto poco si conosce in relazione alle loro caratteristiche e ai rischi che queste comportano per la salute di chi ne fa uso. Oltre a questo, risultano sconosciute anche le modalità analitiche necessarie per riconoscerle in laboratorio e per prevenirne e contrastarne il traffico e lo spaccio sia su territorio italiano, ma anche su quello europeo ed internazionale. Il Sistema Nazionale di Allerta Precoce, istituito nel 2009 presso il Dipartimento Politiche Antidroga della Presidenza del Consiglio dei Ministri, in conformità a disposizioni Europee in materia, monitora la comparsa di tali sostanze sul territorio italiano con lo scopo di individuare precocemente i fenomeni potenzialmente pericolosi per la salute pubblica correlati alla comparsa di nuove sostanze e di nuove modalità di consumo, e di attivare segnalazioni di allerta che tempestivamente coinvolgano le strutture deputate alla tutela della salute e responsabili della eventuale attivazione di misure in risposta alle emergenze.

In recent years we have witnessed a new phenomenon that has revolutionized youth trends, and not just with respect to the use of drugs. To traditional substances (cannabis, cocaine, heroin, etc.) New Psychoactive Substances of synthetic origin have been added, that are still little known with regard to their characteristics and to the risks that they pose to human health. In addition to this, even the analytical methods needed to recognize them in laboratory and to prevent and combat trafficking and smuggling are unknown both on the Italian territory, but also at the European and international level.

The National Early Warning System, established in 2009 at the Department of Antidrug Policies of the Presidency of the Council of Ministers, in accordance with European regulations on the subject, monitors the occurrence of these substances on the Italian territory with the aim to early detect potentially dangerous phenomena for public health related to the appearance of new substances and new methods of consumption, and to enable early warnings that involve the departments responsible for the protection of health and responsible for the eventual implementation of measures in response to emergencies.



Giovanni Serpelloni

Congress Chairman

In considerazione delle sempre più frequenti segnalazioni di Nuove Sostanze Psicoattive che raggiungono il Sistema di Allerta europeo e quello italiano, il Dipartimento Politiche Antidroga ha anche sviluppato un nuovo Piano di Azione Nazionale per la prevenzione, l'identificazione precoce e il contrasto delle Nuove Sostanze Psicoattive.

Questo congresso internazionale, organizzato per la prima volta in Italia, è finalizzato a presentare e a divulgare le informazioni disponibili sul fenomeno delle Nuove Sostanze Psicoattive prendendo in considerazione tutti i diversi aspetti che lo costituiscono e che lo caratterizzano a livello nazionale ed internazionale. L'evento intende fornire evidenze tecnico-scientifiche di alto livello necessarie per affrontare il fenomeno a tutti i livelli e per ampliare la conoscenza di coloro che quotidianamente hanno a che fare con questa problematica.

Per tale ragione, al congresso sono invitati a partecipare operatori dell'ambito analitico, clinico, farmacologico, delle Forze dell'Ordine e della Magistratura.

Tutto ciò affinché si possa costruire una risposta integrata e coordinata tra tutte le amministrazioni ed organizzazioni coinvolte, e poter quindi fronteggiare questa problematica emergente nella salvaguardia della salute dei cittadini.

In view of the increasingly frequent reports of New Psychoactive Substances that reach the European and Italian Early Warning System, the Department of Antidrug Policies has also developed a new National Action Plan for the prevention, early detection and contrast of New Psychoactive Substances. This international conference, organized for the first time in Italy, is designed to present and disseminate available information on the phenomenon of New Psychoactive Substances taking into account all the different aspects that characterize it at national and international level. The event aims to provide evidence of high scientific and technical level necessary to deal with the phenomenon at all levels and to expand the knowledge of those who daily have to deal with this issue.

For this reason, at the conference are invited to participate professionals working in the following fields: analytical, clinical, pharmacological, Law Enforcement and Judiciary.

The aim is to build an integrated and coordinated action across all administrations and organizations involved, and therefore to be able to deal with this emerging public health challenge.

Patrocini Patronages



Ministro della Salute *Minister of Health*



Beatrice Lorenzin

Ministro dell'Interno *Minister of Interior*



Angelino Alfano

Relatori *Speakers*



Giovanni Serpelloni
*Congress chairman -
Italia*



Gilberto Gerra
*United Nations Office
on Drugs and Crime -
Vienna*



Jonathan Lucas
*United Nations
Interregional Crime and
Justice Research Institute
Vienna*



Raymond Yans
*International Narcotics
Control Board - Vienna*



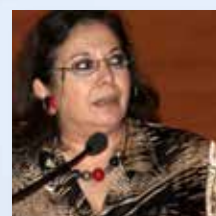
Paul Griffiths
*European Monitoring
Centre for Drugs and
Drug Addiction
Lisbona*



Roumen Sedefov
*European Monitoring
Centre for Drugs and
Drug Addiction
Lisbona*



Moira O'Brien
*National Institute
on Drug Abuse,
Epidemiology Research
Branch - USA*



Teodora Macchia
*Istituto Superiore di
Sanità - Italia*



Bjoern Moosmann
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University Medical
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Giampietro Frison
*Lab. Igiene Ambientale
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Dariusz Zuba
*Institute of Forensic
Research Cracow -
Polonia*



Ettore Zuccato
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Negri" Milano - Italia*



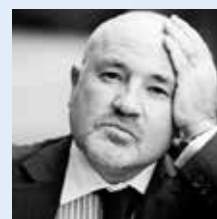
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Pavia Fondazione
Salvatore Maugeri -
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Karen Miotto
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Simon L Hill
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Fabrizio Schifano
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Claudia Rimondo
Sistema Nazionale
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Klaudas Kuchalskis
Europol
Olanda



**Vito Antonio
Diomeda**
Carabinieri per la Tutela
della Salute (NAS) - Italia



Enrico Cataldi
Raggruppamento
Carabinieri
Investigazioni
Scientifiche (RaCIS) -
Italia



Germana Apuzzo
Ministero della Salute
Italia



Donald Hannah
Psychoactive Substances
Regulatory
Authority - Nuova
Zelanda



Ruri Kikura-Hanajiri
National Institute
of Health Sciences -
Giappone



Michal Kidawa
Punto Focale Reitox -
Polonia



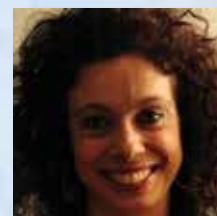
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Michael Baumann
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Franco Tagliaro
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Pirkko Kriikku
Hjelt Institute,
Department of Forensic
Medicine, University of
Helsinki - Finlandia



Maria Augusta Raggi
Università di Bologna
Italia

Moderatori Chairmen

Elisabetta Simeoni	<i>Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri Department for Antidrug Policies, Presidency of the Council Ministers</i>
Elisabetta Bertol	<i>Università degli Studi di Firenze - Dipartimento di Scienze della Salute University of Florence - Department of Health Sciences</i>
Maurizio Gomma	<i>Dipartimento delle Dipendenze Azienda ULSS 20, Verona Addiction Department ULSS 20 - Verona</i>
Giovanni Addolorato	<i>Università Cattolica del Sacro Cuore, Roma - Dipartimento Scienze Mediche Catholic University "Sacro Cuore", Rome - Department of Medical Sciences</i>
Pietro Soggiu	<i>Già Commissario Straordinario per il coordinamento delle Politiche Antidroga Former Special Commissioner for the coordination of Antidrug Policies</i>
Franco Tagliaro	<i>Università di Verona - Dipartimento di Sanità Pubblica e Medicina di Comunità University of Verona - Department of Public Health and Community Medicine</i>
Silvio Garattini	<i>Istituto di Ricerche Farmacologiche "Mario Negri" - IRCCS "Mario Negri" Institute for Pharmacological Research - IRCCS</i>
Daniela Parolaro	<i>Università dell'Insubria - Dipartimento di Scienze Teoriche e Applicate University of Insubria - Department of Theoretical and Applied Science</i>
Claudia Rimondo	<i>Sistema Nazionale di Allerta Precoce - Dipartimento Politiche Antidroga National Early Warning System - Department for Antidrug Policies</i>
Catia Seri	<i>Sistema Nazionale di Allerta Precoce - Dipartimento Politiche Antidroga National Early Warning System - Department for Antidrug Policies</i>
Giordano Biserni	<i>Associazione Sostenitori ed Amici della Polizia Stradale Association of Supporters and Friends of Traffic Police Corps - ASAPS</i>

Programma

Programme

14 Maggio 2014

- 8.30 - 9.30 Registrazione dei partecipanti
 9.30 - 10.00 Saluti delle autorità
Ministro Beatrice Lorenzin

Sessione plenaria

- Moderatore: *Giovanni Serpelloni ed Elisabetta Simeoni*
- 10.00 - 11.00 Il Dipartimento Politiche Antidroga e il Piano d'Azione Nazionale sulle Nuove Sostanze Psicoattive
Giovanni Serpelloni
- 11.00 - 11.30 Nuove Sostanze Psicoattive: un'importante sfida per il sistema sanitario
Gilberto Gerra
- 11.30 - 12.00 Nuove forme di crimine emergente riguardo le NSP e la risposta internazionale
Jonathan Lucas
- 12.00 - 12.30 La responsabilità internazionale nella riduzione del traffico globale di NSP
Raymond Yans
- 12.30 - 13.00 Il ruolo dell'EMCDDA del monitoraggio delle droghe in Europa e il Sistema di Allerta europeo
Paul Griffith e Roumen Sedefov
- 13.00 - 13.30 Community Epidemiology Work Group (CEWG) and Network-Based Models for Monitoring Drug Abuse Trends: le Nuove Sostanze Psicoattive negli Stati Uniti
Maira O'Brien
- 13.30 - 14.30 Pranzo

Sessione I: Aspetti bio-tossicologici: NSP e tecniche analitiche

- Moderatore: *Elisabetta Bertol*
- 14.30 - 14.50 Problematiche analitiche e soluzioni: l'esempio italiano
Teodora Macchia
- 14.50 - 15.10 Agonisti sintetici dei recettori cannabinoidi: metodi di identificazione e conoscenze attuali sulla loro tossicità
Bjoern Moosmann
- 15.10 - 15.30 Potenzialità della spettrometria di massa ad elevata risoluzione ed elevata accuratezza nella caratterizzazione strutturale delle nuove sostanze psicoattive ad azione amfetamino-simile
Giampietro Frison
- 15.30 - 15.50 Delucidazione strutturale delle nuove fenetilamine e triptamine allucinogene identificate sul mercato delle droghe
Dariusz Zuba

May 14th, 2014

- 8.30 - 9.30 a.m. Registration
 9.30 - 10.00 a.m. Opening remarks
Ministro Beatrice Lorenzin

Plenary Session

- Chairmen: *Giovanni Serpelloni and Elisabetta Simeoni*
- 10.00 - 11.00 a.m. The Department of Antidrug Policies and the Action Plan on New Psychoactive Substances
Giovanni Serpelloni
- 11.00 - 11.30 a.m. New psychoactive substances: severe challenges to public health systems
Gilberto Gerra
- 11.30 - 12.00 a.m. New forms of emerging crime regarding NPS and international responses
Jonathan Lucas
- 12.00 - 12.30 p.m. Shared international responsibility in reducing NPS global trafficking
Raymond Yans
- 12.30 - 1.00 p.m. The role of EMCDDA in drug monitoring and the European EWS
Paul Griffith e Roumen Sedefov
- 1.00 - 1.30 p.m. Community Epidemiology Work Group (CEWG) and Network-Based Models for Monitoring Drug Abuse Trends: NPS in USA
Maira O'Brien
- 1.30 - 2.30 pm Lunch

Session I: Bio-toxicological aspects: NPS and analytical techniques

- Chairman: *Elisabetta Bertol*
- 2.30 - 2.50 p.m. Analytical problems and solutions: the Italian example
Teodora Macchia
- 2.50 - 3.10 p.m. Synthetic cannabinoids receptors agonists: methods of detection and current knowledge on toxicity
Bjoern Moosmann
- 3.10 - 3.30 p.m. Capabilities of high resolution/high accuracy mass spectrometry in structural characterization of new psychoactive substances with amphetamine-like properties
Giampietro Frison
- 3.30 - 3.50 p.m. Structural elucidation of new hallucinogenic phenethylamines and tryptamines identified on the drug market
Dariusz Zuba

15.50 - 16.10 L'identificazione delle Nuove Sostanze Psicoattive nelle acque reflue: nuove metodiche e tecnologie
Ettore Zuccato

Sessione II: Aspetti clinico-tossicologici

Moderatore: *Maurizio Gomma e Giovanni Addolorato*

16.20 - 16.40 Problematiche cliniche e soluzioni: l'esempio italiano
Carlo Locatelli

16.40 - 17.00 Aspetti clinici e farmacologici dell'uso dei "sali da bagno"
Karen Miotto

17.00 - 17.20 La tossicità clinica delle fenetilamine PMA/PMMA e NBOMe
Simon L. Hill

17.20 - 17.40 Nuove Sostanze Psicoattive e le implicazioni per la psichiatria
Fabrizio Schifano

17.40 Chiusura lavori della prima giornata

3.50 - 4.10 p.m. The analytical identification of New Psychoactive Substance: new methods and technologies
Ettore Zuccato

Session II: Clinical and toxicological aspects

Chairmen: *Maurizio Gomma and Giovanni Addolorato*

4.20 - 4.40 p.m. Clinical problems and solutions: the Italian example
Carlo Locatelli

4.40 - 5.00 p.m. Clinical and pharmacological aspects of bath salt use
Karen Miotto

5.00 - 5.20 p.m. The clinical toxicity of PMA/PMMA and NBOMe compounds
Simon L. Hill

5.20 - 5.40 p.m. New Psychoactive Substances and the implications for psychiatry
Fabrizio Schifano

5.40 p.m. End of the first day

15 maggio 2014

8.30 - 9.30 Registrazione dei partecipanti

Sessione plenaria: L'organizzazione degli EWS e le nuove modalità di prevenzione dell'offerta online delle NSP

Moderatore: *Pietro Soggiu*

9.30 - 9.50 Introduzione dei lavori
Giovanni Serpelloni

9.50 - 10.10 Il modello organizzativo dell'EWS
Claudia Rimondo

10.10 - 10.30 Ruolo dell'Europol nel contrasto al traffico internazionale di droghe
Klaidas Kuchalskis

10.30 - 10.50 Operazione "Profumo di droga" e altre azioni per il controllo degli smart shop in Italia
Vito Antonio Diomeda

10.50 - 11.10 Identificazione e segnalazione delle sostanze sequestrate sul territorio nei laboratori dei RIS/LASS
Enrico Cataldi

Sessione parallela 1-A: Aspetti normativi

Moderatori: *Franco Tagliaro*

11.20 - 11.40 Aggiornamento delle tabelle delle sostanze soggette a controllo in Italia
Germana Apuzzo

11.40 - 12.00 Le Nuove Sostanze Psicoattive in Nuova Zelanda: un differente approccio di regolamentazione
Donald Hannah (videoconferenza)

12.00 - 12.20 Variazioni nella prevalenza delle Nuove Sostanze Psicoattive prima e dopo l'introduzione della tabellazione generica dei cannabinoidi sintetici in Giappone
Ruri Kikura-Hanajiri

May 15th, 2014

8.30 - 9.30 a.m. Registration of participants

Plenary Session: The organization of the EWS and new ways of prevention against the NPS online offer

Chairman: *Pietro Soggiu*

9.30 - 9.50 a.m. Introduction
Giovanni Serpelloni

9.50 - 10.10 a.m. The EWS organizational model
Claudia Rimondo

10.10 - 10.30 a.m. Europol role in counteracting international drug trafficking
Klaidas Kuchalskis

10.30 - 10.50 a.m. Operation "Scent of a drug" and other measures for the control of smart shops in Italy
Vito Antonio Diomeda

10.50 - 11.10 a.m. Identification and reporting of drugs seized on the territory in RIS/LASS laboratories
Enrico Cataldi

Paralell Session 1-A: Regulatory aspects

Chairman: *Franco Tagliaro*

11.20 - 11.40 a.m. Update of the substances under control in Italy
Germana Apuzzo

11.40 - 12.00 a.m. The new psychoactive substances regime in New Zealand: a different approach to regulation
Donald Hannah (live streaming)

12.00 - 12.20 p.m. Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan
Ruri Kikura-Hanajiri

12.20 - 12.40 La legislazione in Polonia sugli Smart Shops
Michal Kidawa

12.40 - 13.00 Nuove droghe e risk assessment: la proposta italiana
Giovanni Serpelloni

Sessione parallela 1-B: Aspetti farmacologici

Moderatori: *Silvio Garattini e Daniela Parolaro*

11.20 - 11.40 Studi di metabolismo *in vitro* dei cannabinoidi sintetici
Marilyn Huestis

11.40 - 12.00 Effetti farmaco-tossicologici e fisiopatologici di nuove molecole psicoattive sintetiche
Matteo Marti

12.00 - 12.20 Farmacologia dei "sali da bagno" e analoghe droghe sintetiche *Michael Baumann*

12.20 - 12.40 Predizioni del metabolismo *in silico* e *in vitro*: uno studio pilota
Sabina Strano Rossi

13.00 - 14.00 Pranzo

Sessione parallela 2-A: Riduzione della domanda e dell'offerta di NSP via Internet

Moderatori: *Claudia Rimondo e Catia Seri*

14.00 - 14.20 Monitoraggio web e commercializzazione di NSP online: risultati di attività del Sistema Nazionale di Allerta Precoce
Michele Brunetto e Giuseppe Valvo

14.20 - 14.40 Dal NEWS al Law Enforcement: l'oscuramento dei siti web
Francesco Saggio

14.40 - 15.00 Il Deep web: il mercato virtuale delle droghe
Joe Van Buskirk

15.00 - 15.20 Accesso online alle NSP e alle altre sostanze stupefacenti: motivazioni, esperienze, conseguenze per il mercato delle droghe e sfide politiche
Simon Lenton

Sessione parallela 2-B: Incidentalità stradale NSP correlata: le nuove frontiere dell'indagine

Moderatori: *Giordano Biserni*

14.00 - 14.20 Una strategia per bypassare i controlli tossicologici su strada e per il rilascio della patente di guida
Franco Tagliaro

14.20 - 14.40 Prevalenza e concentrazioni ematiche di desossipiradolo (2-DPMP) in automobilisti sospettati di guida sotto l'influenza di droghe e in casi post-mortem
Pirkko Krikkku

14.40 - 15.00 Criticità analitiche per l'identificazione rapida delle NSP su strada
Maria Augusta Raggi

Sessione plenaria: discussione e conclusione

15.20 - 16.00 *Giovanni Serpelloni*

12.20 - 12.40 p.m. The Polish Legislation on Smart Shops
Michal Kidawa

12.40 - 1.00 p.m. New drugs and risk assessment: the Italian proposal
Giovanni Serpelloni

Paralell Session 1-B: Pharmacological aspects

Chairman: *Silvio Garattini and Daniela Parolaro*

11.20 - 11.40 a.m. In vitro metabolism studies of synthetic cannabinoids
Marilyn Huestis

11.40 - 12.00 a.m. Pharmacological, toxicological and pathophysiological effects of new synthetic psychoactive molecules
Matteo Marti

12.00 - 12.20 p.m. Pharmacology of "Bath Salts" and Related Designer Drugs
Michael Baumann

12.20 - 12.40 p.m. In silico and in vitro metabolism prediction: a pilot study
Sabina Strano Rossi

1.00 - 2.00 p.m. Lunch

Paralell Session 2-A: Reduction of NPS internet demand and supply

Chairmen: *Claudia Rimondo and Catia Seri*

2.00 - 2.20 p.m. NPS web monitoring and online marketing: results of N.E.W.S. activity
Michele Brunetto and Giuseppe Valvo

2.20 - 2.40 p.m. From N.E.W.S. to Law Enforcement: the darkening of websites
Francesco Saggio

2.40 - 3.00 p.m. Deep web: the virtual drug marketplace
Joe Van Buskirk

3.00 - 3.20 p.m. Accessing NPS and other drugs online: motivations, experiences, drug market implications and policy challenges
Simon Lenton

Paralell Session 2-B: NPS related road accidents: the new frontiers of the survey

Chairman: *Giordano Biserni*

2.00 - 2.20 p.m. A strategy to pass toxicological tests on the road and for the acquisition of driving licence
Franco Tagliaro

2.20 - 2.40 p.m. Prevalence and blood concentrations of desoxypiradrol (2-DPMP) in drivers suspected of driving under the influence of drugs and in post-mortem cases
Pirkko Krikkku

2.40 - 3.00 p.m. Analytical critical aspects for the rapid identification of NPS on the road
Maria Augusta Raggi

Plenary Session: discussion and conclusion

3.20 - 4.00 p.m. *Giovanni Serpelloni*

Universita' Cattolica del Sacro Cuore *University of the Sacred Heart*



Panoramica della struttura / Overview of the structure



Chiesa Centrale del Sacro Cuore



Auditorium



Centro Congressi Europa

Ministro della Salute / Minister of Health



Min. Beatrice Lorenzin

Ministro dell'Interno / Minister of Interior



Min. Angelino Alfano

I momenti del congresso

Moments from the congress



New Drugs - Piano d'Azione Nazionale / National Action Plan



La libreria espositiva / The expositive bookshelf



Report di attività del Sistema Nazionale di Allerta Precoce / National Early Warning System activity report



Eugenio Valenzi promuove l'Italian Scientific Community on Addiction (ISCA) / Eugenio Valenzi promoting the ISCA



Materiali di prevenzione / Prevention materials

I momenti del congresso

Moments from the congress



I poster delle attività e dei progetti del DPA / Posters of activities and projects by the Department of Antidrug Policies



I poster delle attività e dei progetti del DPA / Posters of activities and projects by the Department of Antidrug Policies



Distribuzione delle cuffie per la traduzione / Distribution of headphones for translation



Raymond Yans e lo staff del Dipartimento / Raymond Yans and the Staff from the Department



Registrazione dei partecipanti / Registration desk



Registrazione dei partecipanti / Registration desk



I poster delle attività e dei progetti del DPA / Posters of activities and projects by the Department of Antidrug Policies



Joe Van Buskirk and Michal Kidawa



Giovanni Serpelloni and General Cataldi



Simon L Hill and Bjoern Moosmann



Da sinistra / From the left: Roumen Sedefov, Paul Griffiths, Raymond Yans, Gilberto Gerra, Giovanni Serpelloni, Daniela Salvati, Elisabetta Simeoni, Moira O'Brien



Da sinistra / From the left: Simon L Hill, Carlo Locatelli, Maurizio Gomma, Giovanni Addolorato, Karen Miotto

I momenti del congresso

Moments from the congress



La platea (di fronte) / The audience (front view)



Da sinistra / From the left: Paul Griffith, Raymond Yans, Gilberto Gerra



Da sinistra / From the left: Klaidas Kuchalskis, Giovanni Serpelloni, Pietro Soggiu, Enrico Cataldi, Claudia Rimondo



Sala Italia - Sessioni parallele / Paralell Session



Gilberto Gerra





Germana Apuzzo



Marilyn Huestis



Veniero Gambaro



Ruri Kikura-Hanajiri



Dariusz Zuba



Moir O'Brien

Abstract dei relatori *Speakers' abstracts*



Giovanni Serpelloni

Congress chairman

Scientific update and National Action Plan on New Psychoactive Substances

Congress Chairman

In recent years, a new phenomenon has revolutionized the youth trends, and not just that, with regard to drug use. To traditional substances, new psychoactive substances (NPS) of synthetic origin were added. Still little is known about NPS with regarding their characteristics and risks for their consumers. Even analytical methods needed to recognize them in the laboratory and to prevent and combat trafficking and smuggling are also unknown. The National Early Warning System, of the Department of Antidrug Policies, monitors the occurrence of these substances on the Italian territory with the aim of early detecting phenomena potentially dangerous to public and health related to the appearance of new substances, and at activating alerts promptly involving organizations responsible for the protection of the health and responsible for the activation of measures in response to emergencies. The Department of Antidrug Policies has developed a National Action Plan for the prevention, early detection and contrast of the NPS. It is based on a balanced and integrated approach, which operates simultaneously on both reduction demand and supply reduction. It also support the promotion of diagnosis, treatment and rehabilitation of consumers, but also a new strategy for combating NPS smuggling and traffic, which has taken on new forms of criminal organization and dissemination via the Internet. It is therefore important to provide technical and scientific evidences to address the phenomenon at all levels and to build an integrated and coordinated response across all administrations and organizations involved in protecting the health of citizens.



Download at <http://allerta.dronet.org/video.html>



Paul Griffiths

*European Monitoring
Centre for Drugs and Drug
Addiction*



Roumen Sedefov

*European Monitoring Centre for Drugs
and Drug Addiction*

The role of the EMCDDA and the EU Early Warning System in the monitoring of new psychoactive substances in Europe

Paul Griffiths and Roumen Sedefov, EMCDDA

The EU Early Warning System on new psychoactive substances (EWS) has been operating for more than fifteen years. The EWS is a near real time vehicle for the exchange of information on new psychoactive substances that may pose public health and social threats.

Now, more than ever, the EWS provides added value to the Member States and the EU Institutions by playing an essential role in ensuring that they have access to the most up-to-date information on new psychoactive substances both from across Europe and beyond. Over the past few years Europe has seen an unprecedented growth in the number, type and availability of new psychoactive substances. In 2013, for the fifth consecutive year, a record number of 81 substances were detected and reported for the first time via the EWS. This represents the largest number of substances ever reported in a single year – more than two thirds of the total number of substances monitored through the system has been identified in the last four years.

Further, where necessary, the system allows for the progression through the scientific risk assessment phase to control measures across the EU. Recently, the EMCDDA has assessed the risks posed by AH-7921 (a synthetic opioid), 25I-NBOME (a potent hallucinogenic phenethylamine sold as LSD), methoxetamine (an arylcyclohexylamine advertised as a 'bladder friendly' alternative to, and sold as ketamine) and MDPV (a ring-substituted synthetic cathinone).

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Bjoern Moosmann

Institute of Forensic Medicine - University Medical Center Freiburg

Synthetic cannabinoid receptor agonists: Methods of detection and current knowledge on toxicity

Bjoern Moosmann and Volker Auwärter, Institute of Forensic Medicine, University Medical Center Freiburg, Germany

Products containing synthetic cannabinoids receptor agonists continue to be widely abused as substitutes for cannabis and almost weekly new substances were identified in the last years. Most of the drugs can be detected in blood or serum as soon as reference standards are available. However, for abstinence control in many environments urine is the preferred test material. For effective urine screening methods the main metabolites of the drugs are the analytical targets, because only very low concentrations of the parent compounds are usually present in urine samples due to extensive metabolism. From a clinical point of view it is evident that these products can cause intoxications much more severe than typical intoxications caused by cannabis use, which is in part due to the high potency and efficacy of the drugs but could also be a consequence of metabolism with a number of metabolites retaining both strong binding affinity and intrinsic activity at the CB1 receptor. Furthermore, as the plant material is either sprayed with or soaked in a drug solution, one main problem arises from inhomogeneities of the 'herbal mixtures' regarding the amount of active ingredient per packet and the distribution within the mixtures. As a consequence, it is not possible for the consumer to safely dose these drugs, and even two joints prepared from the same mixture could contain significantly different amounts of the active substance. Additionally, the compositions of these 'herbal mixtures' change rapidly over time and as a result, a certain product name does not guarantee the same composition of compounds between batches. This poses an additional risk on drug users due to the variability of potency and efficacy of the different compounds. Given the high frequency of appearance of new compounds and the huge variety of chemical substructures, keeping up with identifying and sensitively detecting these analytes or their metabolites presents a continuous challenge for clinical and forensic toxicologists. It is of great importance to meet this challenge, because applying comprehensive drug testing procedures seems to be more effective with regard to demand reduction than enforcement of narcotics law.

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Giampietro Frison

Lab. of Environmental Hygiene and Forensic Toxicology (LIATF), Department of Prevention ULSS 12 Veneziana, Mestre

Capabilities of high resolution/high accuracy mass spectrometry in structural characterization of new psychoactive substances with amphetamine-like properties

Giampietro Frison - Laboratory of Environmental Hygiene and Forensic Toxicology (LIATF), Department of Prevention, Azienda ULSS 12 Veneziana, Mestre - Venezia

Many clinical and forensic toxicology laboratories had to face, in these last years, the analytical challenge represented by the appearance in the illicit market of many new psychoactive substances, with amphetamine-like (cathinones, phenethylamines, piperazines, tryptamines) or cannabis-like properties. To this end several analytical techniques, based on chromatography - mass spectrometry, are currently employed in our laboratory, in particular ultra-high-pressure liquid chromatography coupled to high resolution/high accuracy Orbitrap® mass spectrometry (UHPLC-HRMS). The capabilities of UHPLC-HRMS in elucidating elemental composition and structural characteristics of new psychoactive drugs with amphetamine-like properties are described. The UHPLC-HRMS analytical strategy is based on: 1) efficient chromatographic resolution of analytes; 2) study of MH⁺ collision-induced product ions obtained in MS/MS experiments; 3) accurate mass measurements of MH⁺ ionic species in full scan conditions; 4) comparison of experimental and calculated MH⁺ isotopic clusters; 5) examination of the isotopic fine structure of the M+1, M+2, M+3, M+4 isotopic peaks relative to the monoisotopic (M+0) peaks. The UHPLC-HRMS analytical approach has allowed our laboratory to identify so far, even without availability of reference standards, about 25 new psychoactive substances with amphetamine-like properties found in seized materials, and in some cases even in biological samples.



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Dariusz Zuba

Institute of Forensic Research Krakow

Structural elucidation of new hallucinogenic phenethylamines and tryptamines identified on the drug market

Dariusz Zuba - Institute of Forensic Research, Westerplatte 9, 31033 Krakow, Poland

Phenethylamines and tryptamines are two broad groups of psychoactive substances that produce a range of hallucinogenic effects. These compounds have a long history of licit use for spiritual and medicinal purposes (e.g., dimethyltryptamine (DMT) is an active ingredient of *Banisteriopsis caapi* used to make Ayahuasca decoctions, while MDMA was a medicine in psychotherapy). Phenethylamines and tryptamines have also been used for recreational purposes by young people in club and rave environments. The Internet has facilitated the illicit use in recent years, as these substances can be purchased from internet stores selling them as research chemicals, bath crystals or plant food.

Unequivocal identification of phenethylamines and tryptamines is a big challenge. The main reason is a rapid growth in the number of substances detected on the drug market. According to reports of the European Monitoring Centre for Drug and

Drug Addiction (EMCDDA), 70 phenethylamines and 28 tryptamines were notified through the early warning system. The similarity in chemical structures between different representatives causes that common analytical techniques used in forensic laboratories often fail and the use of sophisticated hyphenated methods is required. Gas chromatography – mass spectrometry (GC-MS) has become the standard screening tool with a growing number of records in the mass spectral databases. But the findings have to be interpreted with care and supported by other experiments, including derivatisation, e.g. with trifluoroacetic anhydride (TFAA), the use of chemical ionization or high-resolution mass spectrometric techniques, e.g. liquid chromatography – quadrupole time-of-flight mass spectrometry (LC-QTOFMS). Application of Fourier-transform infrared spectroscopy (FTIR) is recommended when different positional isomers are considered. A new substance is usually characterized by nuclear magnetic resonance (NMR) spectrum, but this technique has the limitations concerning amount and purity of the sample.

Schemes used for identification of new psychoactive substances in elementary and advanced laboratories will be presented. Benefits and pitfalls of different analytical methods will also be discussed in the lecture.

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Ettore Zuccato

Istituto di Ricerche Farmacologiche "Mario Negri" Milano

Detection of New Psychoactive Substances in wastewater: new methods and technologies

Ettore Zuccato, Sara Castiglioni - IRCCS "Mario Negri" Pharmacologic Research Institute, Via Giuseppe La Masa 19, 20156 Milan

A new estimation method on NPS consumption in the general population has been recently set. It is based on wastewater analysis (Zuccato et al., 2005). The principle on which this method is based is that when a consumer takes a substance, this is absorbed, metabolized and eventually excreted through urines and faeces. Wastewater therefore keeps track of all the substances that have been collectively consumed by the population. So far, the wastewater analysis has allowed to estimate consumption of the so called "classic" psychotropic substances such as cocaine, amphetamine, heroine and cannabis (Zuccato et al, 2008).

This method could be easily adapted for the evaluation of NPS consumption. If some of these substances became of common use by a sufficiently numerous group of subjects, it would be possible to measure their traces (metabolites or residuals of parental substances) in wastewater. The method would be then suitable for estimating which, amid all the new identified substances that are marketed (also online), seized or cause of admission in Emergency Departments are actually consumed by the population not just occasionally but on a regular basis and in a remarkable level. That means to be able to identify which, among hundreds of potential substances, have in fact become "of common use".

To achieve this research goal, we are testing a specific software called "Trace finder", which applies hi-tech solutions for the identification of unknown substances in environmental samples (e.g. urban wastewater). The chemical characteristics either of parental substances or of known or presumed metabolites (exact mass, mass/charge ratio, isotopic fragments, isotopic patterns, retention times) of Psychoactive Substances concur to build a dataset which is then used to identify these substances in wastewater by means of mass spectrometry techniques. Analytical standards, when available, allow to build mass/mass spectra libraries that are then applied so as to identify these substances in wastewater. The software has been used for the analysis of ketamine and mephedrone and there are ongoing studies for the analysis of other NPSs in wastewater of some Italian cities.

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Carlo Locatelli

Centro Antiveleni di Pavia Fondazione Salvatore Maugeri

New Psychoactive Substances (NPS) clinical problems and solutions: the Italian example

Carlo Alessandro Locatelli - Centro Antiveleni di Pavia - Centro Nazionale di Informazione Tossicologica, IRCCS Fondazione Maugeri, Pavia

The management of a patient intoxicated by NPS neurotoxic effects presents some critical issues, both in the pre-hospital and in the hospitalization phase, such as (a) the management priorities in the early stages, (b) the specific toxicological (clinical and analytical) diagnosis (c) the choice of the most suitable (clinical and / or instrumental) monitoring, (d) the type of treatment in emergency (short observation, emergency medicine, SPDC, other departments), and (e) the criteria to be assumed for the discharge or the admission to at lower-intensity wards. The process of diagnosis is often complex. Patients entering the emergency departments for NPS acute intoxication not usually have a history of abuse. From the clinical toxicology standpoint, they could be classified into two main types, each characterized by different levels of severity: patients with prevalent neurodepression (eg, psychomotor decline, coma) and patients with prevalent neuroexcitatory effects (agitation, delirium, hallucinations, etc.). To better understand and assess the NPS issue, to improve diagnosis, to identify new syndromes and analytical needs in the urgency system and, more generally, to cope with this new toxicological and social emergency, in Italy urgent and special measures have been taken in coordination with the Department for Antidrug Policy of the Presidency of the Council of Ministers. The National Early Warning System (www.allertadroga.it) is indeed a network of emergency services of the NHS which includes laboratories, poison control centers and other resources that work quickly to coordinate the necessary activities, information, alerts and other useful functions to deal with this issue. Through this network toxicological expertises and analytical abilities are made available for the urgency system with the aim of early identify and confirm NPS poisoning. In this context, the Poison Control Center toxicological specialists play a central role in the diagnosis and the setting of specific treatments, in the choice of the most appropriate placement of the patient in the acute phase (eg, indicated and contraindicated drugs), for the assessment of analytical needs in urgency, as well as specialized reference to the post-acute non-psychiatric phase.

Acknowledgements: The study has been carried out with the support of the National Early Warning System, Department for Antidrug Policy of the Presidency of the Council of Ministers, 2011-2013.

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Karen Miotto

School of Medicine at UCLA, Semel Institute of Neuroscience and Human Behavior - Los Angeles

Bath Salts

Karen Miotto - School of Medicine at UCLA, Semel Institute of Neuroscience and Human Behavior - Los Angeles

A new emerging drug commonly known as "bath salts" has recently gained extensive popularity. This synthetic cathinone yields many adverse effects similar to stimulants. Although bath salts have only been prevalent for several years, their potent harmful effects have been medically recognized. Consumers often experience a range of acute psychosis and cardiovascular symptoms, such as paranoia, hallucinations,



panic attacks, chest pains, heart palpitations, etc. This presentation will delve further into the adverse psychiatric effects of bath salts and its management in a clinical setting.

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Fabrizio Schifano

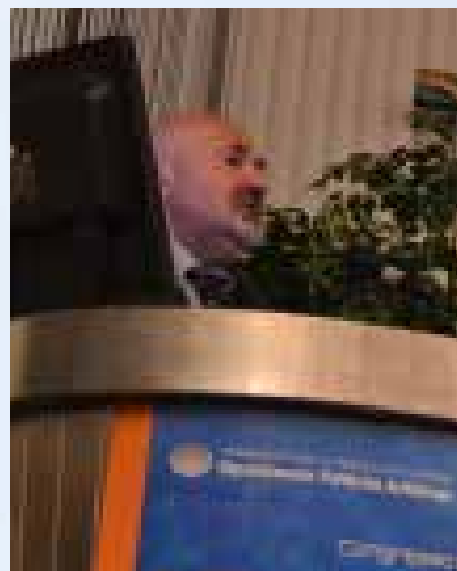
School of Pharmacy, University of Hertfordshire, UK

NPS, clinical pharmacological and psychopathological issues

Fabrizio Schifano - School of Pharmacy, University of Hertfordshire, UK

Prof. Fabrizio Schifano (MD, FRCPsych) will provide an overview of the clinical pharmacological and toxicity challenges posed by a range of Novel Psychoactive Substances, including: psychedelic phenethylamines; synthetic cathinones, synthetic cannabimimetics; PCP-like drugs; and herbs/plants' derivatives. He will comment as well on the clinical issues relating to the misuse of a range of prescription drugs, including gabapentinoids and anticholinergics.

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Claudia Rimondo

Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga

The Early Warning System organizational model

Claudia Rimondo - National Early Warning System - N.E.W.S.

The Italian National Early Warning System (N.E.W.S.) of the Department for Antidrug Policies, Presidency of the Council of Ministers, was established in 2009 with the aim of monitoring the presence of New Psychoactive Substances (NPS) in Italy and of collecting information on their patterns of use and toxicological effects.

The NPS phenomena is monitored through the collection of notification (information on seizures, collected samples or clinical cases) coming from law enforcements, toxicology laboratories, clinical/emergency departments, etc., belonging to the N.E.W.S. Collaborating Centre Network. Data are processed to activate alerts and produce technical folders shared with the N.E.W.S. Network to improve the awareness and knowledge on NPS spread in Italy and Europe.

The N.E.W.S. involves 130 Collaborative Centres. Notifications of NPS registered by the N.E.W.S. for the first time in Italy resulted in a high number of new synthetic cannabinoids (30), cathinones (15) and phenethylamines (20). Since 2010, 43, 8 and 17 acute intoxication cases, related respectively to synthetic cannabinoids, cathinones and methoxetamine, were also notified. Web monitoring started in 2011 and allowed the reporting of 523 Internet pages to the Law Enforcement, 93,8% no more visible.



The spread of NPS is hard to evaluate due to unavailability of standard compounds, lack of specific analytical methods and unavailability of primary rapid screening tests in case of intoxications. Data sharing provided by the N.E.W.S. allowed the Collaborative Centres to be updated in real time on the appearance of NPS, to improve their analytical ability to rapidly identify NPS and to promptly make diagnosis, indicating that the working method used is valid, reliable and effective.

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Klaudas Kuchalskis

Europol

Europol role in counteracting international drug trafficking

Klaudas Kuchalskis - Europol

Please be informed that that Europol's presentation will focus on combating NPS from the law enforcement perspective, in particular:

- Situation in the EU (SOCTA 2013 findings concerning NPS)
- Common threats
- NPS production and trafficking
- Crime relevant factors
- Intelligence gaps
- Law enforcement response/role of Europol
- Early Warning System: law enforcement component
- EMPACT priority on synthetic drugs
- Law enforcement limitations
- Europol support
- Case study.

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Vito Antonio Diomeda

Carabinieri per la Tutela della Salute (NAS)

N.A.S. and the New Psychoactive Substances

Colonnello Vito Antonio Diomeda - Vice Comandante dei Carabinieri per la tutela della Salute (N.A.S.)

- Origin, articulation and institutional tasks of N.A.S.
- N.A.S. and "Smart Drugs – NPS"
- Law enforcement activities concerning NPS
 - Criminal organizations' modus operandi;

- Major criminal investigations;
- Collaboration with the Department for Antidrug Policies of the Presidency of the Council of Ministers;
- Stores selling smart drugs on the territory;
- NPS and the web: a preview

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Enrico Cataldi

Raggruppamento Carabinieri Investigazioni Scientifiche (RaCIS)

Detection and notification of New Substances that have been seized on the territory by scientific Units (RIS/LASS) of Carabinieri Law Enforcement

Generale Enrico Cataldi - Raggruppamento Carabinieri Investigazioni Scientifiche (RaCIS)

In the last years, we have witnessed a new phenomenon which has revolutionized youth trends on drug abuse. Together with the consumption of "traditional" illicit drugs such as cocaine, cannabis, amphetamines and their derivatives, a new social emergency has raised, namely the spread of the so called "smart drugs", new synthetic substances which are characterized by similar or even worse effects on human health than the "traditional" drugs. The fight against this phenomenon cannot be separated by the ability of chemical-analytical identification of these substances and by their early notification to the National Early Warning System of the Department of Antidrug Policies (N.E.W.S.) in order to allow the prompt identification of suitable countermeasures both at a local and national level and to permit the constant update of the list of illicit substances. In order to tackle this phenomenon, the Carabinieri law enforcement corp has a technical-scientific unit (Raggruppamento Carabinieri Investigazioni Scientifiche) which is composed by 4 RIS (Scientific Investigation Detachments) each having an interregional jurisdiction and by 29 Laboratori per Analisi di Sostanze Stupefacenti - LASS (Laboratories for the analysis of narcotic substances) each having a provincial jurisdiction. They all assure a widespread NPS identification capacity on seizures carried out by Law Enforcement.

The collaboration between the Raggruppamento Carabinieri Investigazioni Scientifiche (RaCIS) and the Department of Antidrug Policies of the Presidency of the Council of Ministers forms part of such framework. The constant technical-operative update of the laboratory specialized personnel led to the achievement of remarkable results in terms of a more and more effective identification and chemical-analytical characterization of NPSs and/or of abnormal "classical" drug samples. After the end of this first "RIS-NEWS" course, an increase in the quality-quantity of alerts to the National Early Warning System - N.E.W.S. has been registered. In fact, there have been 189 alerts made by the RIS and LASS corps from April 2013 to April 2014, compared with just 32 alerts that had been reported in 2012.



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Ruri Kikura-Hanajiri
National Institute of Health Sciences - Japan

Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan

Ruri Kikura-Hanajiri - Section Chief, Division of Pharmacognocny, Phytochemistry and Narcotics, National Institute of Health Sciences, Tokyo 158-8501, Japan

To counter the spread of the many analogs of psychoactive substances, the Pharmaceutical Affairs Law in Japan was amended in 2006 to establish a new category; "Designated Substances" in order to more promptly control these drugs. However, new analogs of controlled substances, especially synthetic cannabinoids and cathinone derivatives, appeared one-by-one. To avoid a cat-and-mouse game, a comprehensive system (generic scheduling) for designating the naphthoylindole-type synthetic cannabinoids and the cathinone derivatives was introduced into the "Designated Substances" in 2013 and 2014.

We investigated the distribution of synthetic cannabinoids before and after their control in Japan during the last six years. Until 2011, the synthetic cannabinoids having only four structures (cyclohexylphenols, naphthoylindoles, phenylacetylindoles and benzoylindoles) had been detected in products and 63% of the compounds detected from 2009 to 2011 were the naphthoylindoles. MAM-2201 was the most frequently detected in 2012. On the other hand, since 2012, new types of synthetic compounds, such as cyclopropylmethanones (e.g. UR-144 and XLR-11), carboxyamides (e.g. APICA and APINACA) and quinolinyl carboxylates (e.g. PB-22) have increased. In particular, after the enforcement of the generic scheduling for designating naphthoylindoles in March 2013, the naphthoylindoles have been completely replaced by other types. 5-Fluoro PB-22 (in early 2013) and FUB-PB-22 (in the second half of fiscal 2013) were the most detected synthetic cannabinoids in the product after the generic scheduling. Based on our studies on the binding affinities of newly-emerging synthetic cannabinoids at the cannabinoid CB1 and CB2 receptors, these new compounds have high CB1/CB2 receptor binding affinities. Although the binding affinities at the CB1/CB2 receptors do not directly reveal each neuro-pharmacological activity, their potential health damage is expected.

Because information sharing among laboratories is the key to a fight against these new psychoactive substances, we opened "Data Search System for New Psychoactive Substances" (http://npsdb.nihs.go.jp/Search/Default_e.aspx) on the web site in March 2014. To avoid health problems and abuse caused by new designer drugs, we have to continuously monitor the distribution of these products.

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Michał Kidawa
Reitox Focal Point - Poland

The Polish Legislation on Smart Shops

Michał Kidawa - National Early Warning System, National Focal Point, National Bureau for Drug Prevention

Poland was one of the countries where legal high phenomenon developed very rapidly. In two years (from 2008 to 2010) the number of street shops offering new psychoactive substances increase from 40 to over 1300, despite legal efforts to stop the

phenomenon (like delegating large number of substances). At the end of 2010 the new act of law was passed. Act banned manufacturing or introducing to trade so called substitute drugs (legal highs). Violating the ban on introducing substitute drugs to trade is subject to fine ranging from PLN 20 000 to 1 000 000 (~5.000 – 260.000 euro). The main objective of this presentation is to present the consequences and impact of legal changes on the drug scene and legal high phenomenon. An analysis of available sources have been done. Statistics of poisoning cases and surveys from the years 2010 and 2013 were analyzed. The recent survey "Youth 2013" shows that the legal change from 2010 was followed by significant decrease of prevalence of experiments with legal highs among Polish youth. The live time prevalence of legal highs use has decreased from 11,5% in 2010 to 3,5% in 2013. On the other hand undesirable side effects to public health of the implemented in the 2010 legal changes have been noted. Additionally, some aspects of the law proved to be difficult to implement in current form.

Although the legal changes of drug law from the 2010 is still being considered as a success, negative side effects and difficulties in the law implementation were noted. This is why in the 2013 the team of experts started to develop recommendations for new amendment of the law. Basing on this the amendment was prepared. The amendment is still in the interministerial consultations. The concept of changes and idea behind new legislation will be also included in the presentation.



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Matteo Marti

University of Ferrara

Pharmaco-toxicological and physio-pathological effects of New Synthetic Psychoactive molecules

Department of Life Sciences and Biotechnology (SvEB), University of Ferrara, Italy, Center for Neuroscience and Collaborating Center for the Italian National Early Warning System

K2 or Spice products became popular in 2008 as drugs of abuse [1] and are illegally marketed for their psychoactive effects similar to those produced by cannabis [2]. These "herbal" preparations contain varying amounts of different synthetic cannabinoids (SCBs) that showed high affinity for CB1 and CB2 receptors. Although assumed by many teens and first time drug users to be a "safe" and "legal" alternative to marijuana, many recent reports indicate that SCBs create a serious public health issue due to medical and psychiatric toxicities [3, 4] that seems not associated with the primary psychoactive component of marijuana, Δ^9 -tetrahydrocannabinol (Δ^9 -THC). In particular, seizures, hyperreflexia, myoclonias and cardiac toxicity appear to be the main "atypical" side effects observed in emergency rooms [3, 4]. In the present preclinical study we evaluated the pharmaco-toxicological effects in mice of JWH-018 and 5F-AKB, 5F-ADBINA 5F-PB 22, three novel fluorinated SCBs, recently seized in the Internet market. SCBs were studied using a battery of behavioral tests widely used in studies of "safety-pharmacology" for the preclinical characterization of new molecules [5]. In order to compare the behavioral and pharmacological effects induced by SCBs in mice we used as a reference compound the Δ^9 -THC (Dronabinol®). We demonstrated that all SCBs reproduced the typical cannabinoid "tetrad" in mice characterized by hypolocomotion, catalepsy, hypothermia and acute analgesia. A significant effect is observed in the inhibition of the visual and auditory sensory reflex. In fact, SCBs (5F-PB 22 \geq JWH-018 > 5F-ADBINA \geq 5F-AKB) inhibited more readily and with greater effectiveness than THC visual and auditory sensory responses of the mouse. Moreover, the effects are long lasting and persist beyond the 5 hours of observation. The compounds also alter the sensorimotor



responses in reply to tactile stimuli (corneal, vibrissae, pinnae reflex), although less intensively compared to those observed on visual and auditory reflexes. Regarding the main neurological effects, it is interesting to note that the administration of SCBs (5F-PB 22 > 5F-AKB > JWH-018) induced myoclonus, hyperreflexia and seizures in mice. Moreover, SCBs (5F-AKB > JWH-018 > 5F-PB 22) induced relevant long-lasting (up to 5 hs) cardio-respiratory changes characterized by deep bradycardia (heart rate reduction of about 50 %) alternated with episodes of tachyarrhythmias. Cardiac effects were accompanied by bradypnea (breathing rate reduction of about 50 %) and mild reduction in SpO₂ (SpO₂ reduction of about 25 %). For the first time the present study reproduced in the mouse model the “atypical” side effects induced by SCBs in humans as seen in emergency rooms, and it strengthens the pre-clinical evidence on the health hazard represented by SCBs.

Acknowledgments. This research has been funded by the Drug Policies Department, Presidency of the Council of Ministers, Italy (project NS-Drugs to M Marti).

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Michael Baumann

Intramural Research Program, National Institute on Drug Abuse

Pharmacology of “bath salts” and their newly-emerging analogues

Michael H. Baumann, PhD - Designer Drug Research Unit, IRP, NIDA, NIH, Baltimore, MD 21224

The abuse of synthetic cathinones, or so-called “bath salts”, is a growing public health concern. Common constituents of bath salts, including 3,4-methylenedioxypyrovalerone (MDPV) and 4-methylmethcathinone (mephedrone), have been rendered illegal, but new cathinones are being marketed as replacements. The purpose of the present investigation was to examine the interaction of newly-emerging cathinones with transporters for dopamine (i.e., DAT) and 5-HT (i.e., SERT). Derivatives of MDPV that were studied include α -pyrrolidinovalerophenone (α -PVP), while derivatives of mephedrone include 4-methylethcathinone (4-MEC) and 4-methylpyrrolidinopropiophenone (4-MePPP). In vitro assays were carried out in rat brain synaptosomes to assess drug-induced effects on transporter-mediated uptake and release. In vivo microdialysis was carried out in rat nucleus accumbens to assess drug-induced changes in extracellular dopamine and 5-HT. MDPV and α -PVP displayed low nM potency as DAT blockers. Mephedrone was a non-selective transporter substrate with releasing ability at DAT ($EC_{50} = 38$ nM) and SERT ($EC_{50} = 98$ nM). 4-MEC had unusual properties, blocking uptake at DAT ($IC_{50} = 546$ nM) while evoking release at SERT ($EC_{50} = 123$ nM). 4-MePPP (1.0-3.0 mg/kg, i.v.) selectively increase extracellular dopamine, whereas mephedrone and 4-MEC (1.0-3.0 mg/kg, i.v.) elevate dopamine and 5-HT. Each of the compounds examined displays a unique profile of in vitro transporter activity. Pyrrolidinophenones like MDPV and α -PVP are potent DAT blockers. Increasing the N-alkyl chain length of mephedrone creates compounds with reduced releasing activity, converting them to DAT blockers. In vivo findings demonstrate that all of the newer replacement cathinones increase extracellular dopamine to some extent, suggesting these drugs possess a significant risk for abuse.

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Sabina Strano Rossi

University of "Sacro Cuore" - Rome

In silico and in vitro metabolism prediction: a pilot study

Sabina Strano Rossi - Istituto di Sanità Pubblica - Sezione di Medicina Legale, Università Cattolica del S. Cuore Roma

Between 2009-2012, EMCDDA reported the identification of 200 new psychoactive substances (NPS) in the illicit market; in August 2013, the National Early Warning System pointed out more than 280 NPS. These substances belong to different chemical classes, recently classified by UNODC in synthetic cannabinoids, synthetic cathinones, ketamine, phenethylamines, piperazines, substances not belonging to any of these classes, and vegetable ones. The phenomenon involves issues of public security and citizens health. In this context, health protection units (Emergency Department and Poison Control Centers) and academic research institutions (Forensic Toxicology) have a key role for the prompt identification of NPS and their metabolites in intoxicated/dead subjects' biological samples and subsequent reporting to the National Early Warning System (EWS). Therefore, it is essential to develop analytical methods capable of detecting NPS, their metabolites or biomarkers of abuse, in consumers' biological samples or in intoxicated/died subjects. Many of the papers published are related to the experimental study in vitro metabolism of NPS, primarily synthetic cannabinoids, because the unchanged compounds are usually not detected in urine after consumption. A further approach is the theoretical computational prediction (in silico) of metabolites, depending on the molecular structure, on the reactivity of its sites and on its possible interaction with the enzyme that catalyzes the metabolic reaction. In vitro metabolism experiment, coupled with in silico prediction, are therefore an important and working alternative to human studies.

The speech describes possible methods for the identification of NPS markers of abuse in biological fluids, mainly urine, whereas it is impossible to carry out studies on volunteers, given the potential dangers of the substances tested.

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Francesco Saggio

Nucleo Antisofisticazione - Arma dei Carabinieri

Closing illicit web sites

Capitan Francesco Saggio - Comandante del Reparto Analisi dei N.A.S.

- Origins of the collaboration with the Department for Antidrug Policy of the Presidency of the Council of Ministers
- Darkening, inhibition and elimination of websites offering NPS and related law enforcement activities
 - NPS advertisements and law enforcement activities;
 - Domains which sell NPS and law enforcement activities;
 - Modus operandi of organizations managing websites and illegal advertisements;
- Police's difficulties in law enforcement activities against NPS

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Giuseppe Valvo

European Institute for Health Promotion


Michele Brunetto

European Institute for Health Promotion

Web monitoring - Prevention of online drug sales and illegal rave parties

Giuseppe Valvo and Michele Brunetto - European Institute for Health Promotion

Internet gives the opportunity to access quickly and easily to a wide number of information and to start a commercial relations for any kind of product, including unfortunately drugs. In this context, the Department for Antidrug Policies has activated a web monitoring unit, within the National Early Warning System which operates with the aim to identify and to obtain information on these phenomena and to prevent that users purchase and consume the substances sold on the web and the darknet. The web monitoring takes place within standardized procedures shared with the Central Directorate for Anti-drug Services and Carabinieri N.A.S. The methods are based on research of websites in Italian language or with server located in Italy, easily accessible to any user interested to purchase illicit drugs. For Deep Web, the monitoring unit has highlighted the features of this "invisible web", through specific software. Finally, for the illegal rave parties, the web monitoring unit send a notification to the Law Enforcement of the presence of any illegal rave parties, promotion on the web.

From July 2011 to April 2014, 544 web pages selling New Psychoactive Substances



(NPS) were notified to the law enforcement. Of reports to the Carabinieri N.A.S. of sites which sell controlled substances, 66.9% resulted in the removal of the notice and in 22.8% of cases the web page was closed. The site notified was closed in 1.3% of cases. Only 9.0% of the pages notified are still visible on the web. For deep web, have been identified 39 web sites that sell illegal drugs. Finally, the monitoring activity conducted from October 2010 to April 2014 also led to the identification of 139 illegal music events promoted online. 136 of these were notified by the Prefecture, Police, municipality and referred to the Magistrate of the place where the event was to be held and the Central Executive for Anti-Drug Services, in order to verify the legitimacy of the organisation. 43 of these (30.9%) were prevented, i.e. closed before taking place; 37 were managed by intervention in loco of the Police forces (26.6%); 39 (28.1%) took place in spite of the notification. 17 events are waiting for report; 3 events indicated as not reported, are events where insufficient advance information regarding the place has been collected and therefore they have not been notifiable to the Police forces and to the regional administrations. The web monitoring proves to be a useful and effective tool to examine aspects of the phenomenon of supply of illegal drugs via the Internet. In terms of health, the web monitoring can reduce the availability of toxic substances to the health of consumers, thus decreasing the possibility that they may incur in cases of intoxication or situations that could endanger their health, their lives and the lives of the people close to them.



Download "ongoing"



Joe Van Buskirk

National Drug and Alcohol Research Centre - University of New South Wales - Sydney

Monitoring Dark Web Marketplaces – After the Silk Road

Joe Van Buskirk¹, Amanda Roxburgh¹ and Lucinda Burns¹

¹National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia

Issue: The closure of the Silk Road in October 2013 led to much discussion online of alternate dark web marketplaces on which to trade illicit substances. In the absence of any one marketplace emerging to take its place, and the closure of many alternative online markets due to fraud or security vulnerabilities, multiple marketplaces are now regularly monitored.

Approach: Dark web marketplaces were first identified and monitored weekly for changes in size and the availability of substances being sold. Details on retailer numbers, the substances for sale, as well as the countries of origin and shipping destinations for these substances, were collected and analysed over time. The data from seven different marketplaces of varying sizes and lifetimes are presented.

Key Findings: Marketplaces varied in the proportion of Australian domestic retailers, as well as international retailers willing to ship to Australia. An upward trend over the monitoring period was observed among both Australian and international retailer categories. Australian retailers on the Silk Road 2.0 in particular have increased markedly. The specific substances available across marketplaces varied less, with cannabis, MDMA and pharmaceutical drugs most commonly sold, with slight variations in rank. Some marketplaces had a slightly higher availability of new psychoactive substances, but largely the substances for sale mirrored street availability identified in other Australian and international monitoring systems.

Implications: The increasing proportion of Australian retailers operating on the Silk Road 2.0 requires ongoing monitoring. Despite data from the Ecstasy and related Drugs Reporting System suggesting that this group of consumers prefer to purchase their drugs from more traditional sources (e.g. through friends and known dealers), dark web marketplaces have the potential to influence the price, purity and availability of drugs in traditional street marketplaces should their reach broaden out. Given the findings from this research, dark web marketplaces appear likely to continue operating.

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Simon Lenton

National Drug Research Institute

Accessing NPS and other drugs online: motivations, experiences, drug market implications and policy challenges

Simon Lenton PhD (presenting), Monica Barratt PhD, Alexia Maddox PhD

National Drug Research Institute - Curtin University, GPO Box U1987 Perth WA 6845 - Australia

This paper draws on data from recent quantitative and qualitative studies of drug users who use the internet to access drugs or drug information online to consider their motivations for and experiences of sourcing NPS and other drugs online. Data shows

that although NPS are not the most frequently accessed drugs, there are between country differences which probably reflect local drug market factors. Similarly motivations for buying drugs on line are varied with the variety of drugs available, quality, convenience and the confidence provided by on-line seller rating schemes are commonly mentioned factors. The dynamic nature of the online drug market places, including the impact of drug law enforcement actions and responses to these, means this aspect of the NPS story is one that is rapidly changing. The paper will consider issues around public health, harm reduction, drug market implications and policy challenges.

Download "ongoing"



Pirkko Kriikku

Hjelt Institute, Department of Forensic Medicine, University of Helsinki

The role of the new stimulant designer drug desoxypipradrol (2-DPMP) in driving under the influence of drugs cases and fatalities in Finland

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Desoxypipradrol was originally developed for medicinal use, but in the later stages of its development it was replaced by methylphenidate, a structurally similar molecule currently used for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy. Desoxypipradrol is a very long acting psychostimulant that has been shown to cause serious side effects in some recreational users. It was recently scheduled as an illegal narcotic in the national Narcotics Act in Finland. In this study, the prevalence and serum concentrations of desoxypipradrol in drivers suspected of being under the influence of drugs (DUID) and in post-mortem cases in Finland were assessed. Serum samples from drivers apprehended on suspicion of DUID, and blood/urine samples from post-mortem cases, were analysed for the presence of desoxypipradrol and other psycho active drugs. All samples were analysed by mass spectrometric methods. Between October 2010 and December 2012, there were 107 desoxypipradrol-positive samples from apprehended drivers. In nearly all cases amphetamine and/or benzodiazepines were also present. The median (range) desoxypipradrol concentration in DUID cases was 0.069 mg/L (0.006–0.890 mg/L). In over half of the desoxypipradrol positive cases a clinical examination was carried out by a physician shortly after the arrest and functional impairment was found in more than 43% of these. Of all the post-mortem toxicology cases in the study period, desoxypipradrol was found in 5 cases (0.05% of the investigated cases). The concentration of desoxypipradrol in post-mortem cases ranged between 0.01 and



1.40 mg/L. There is very little information available on the pharmacology and toxicology of desoxypipradrol. In our study, it was only rarely found in post-mortem toxicology. In DUID cases, however, it was the second most common novel designer drug after MDPV. Based on our findings and on the few reports from other studies, it is likely that desoxypipradrol - along with other novel drugs of abuse - has an increasing detrimental impact on traffic safety.

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Maria Augusta Raggi

University of Bologna

Analytical difficulties for nps roadside drug tests

Maria Augusta Raggi - Laboratorio di Analisi Farmaco-Tossicologica, Dipartimento di Farmacia e Biotecnologie, Alma Mater Studiorum-Università di Bologna, Via Belmeloro 6, 40126 Bologna

It is scientifically proven that the use of psychotropic substances leads to perceptual distortions that negatively affect complex tasks such as driving. That highlights the need for rapid and reliable analytical methods to determine the actual NPS consumption among drivers.

Given the lack of analytical methodologies for NPS detection, the Laboratory of Pharmaco- Toxicological Analysis is engaged in the development of new methods, in order to assist roadside drug testing by law-enforcement agencies.

The Laboratory has just proposed an alternative biological matrix, the dried blood spot (DBS), to check substance abuse. Compared to traditional venipuncture, DBS matrix has several advantages: it is very fast and minimally invasive, it allows the immediate blood collection, during police roadside control or after a road accident, showing driver's blood condition. DBS test is a promising strategy for NPS analysis.

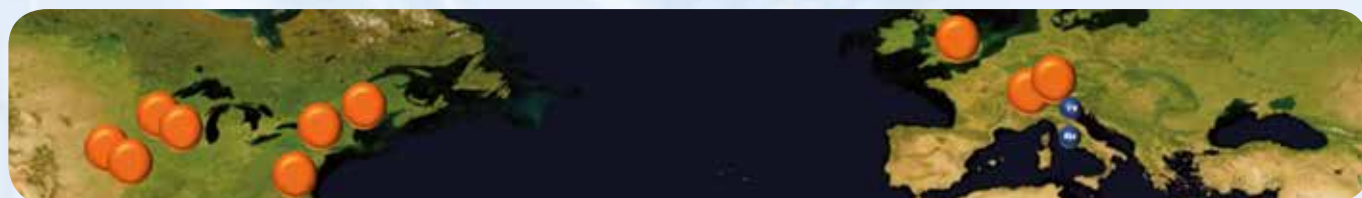
In particular, γ - hydroxybutyric acid (GHB) has placed analytical problems that are not easily solvable, both for its unusual chemical formula, and for its rapid metabolism. The Laboratory is validating a capillary electrophoresis method with indirect detection for the GHB analysis in DBS matrix. Moreover, it's developing analytical methods based on HPLC -F and LC-MS/MS use for ketamine analysis. Ketamine requires high analytical sensitive methods to avoid "false negatives" cases, because it is present in the blood at levels of few ng/mL. The Laboratory is also developing analytical methods for the rapid identification of some synthetic cannabinoids and of fentanyl.

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Poster istituzionali Institutional posters

International collaborations for scientific research



United Nations Office on Drugs and Crime (UNODC), Vienna



UNODC

United Nations Office on Drugs and Crime

Areas of collaboration: Prevention and Training

Activities: This joint initiative aims at supporting the creation of regional hubs connecting and training policy makers from different countries in order to provide them concrete tools to improve their respective national prevention systems, including drug prevention programs and informative materials. The initiative is active in Central America, Northern Africa, Central Asia and East Asia.

National Institute on Drug Abuse, Bethesda, USA



**NATIONAL INSTITUTE
ON DRUG ABUSE**

Areas of collaboration: Early diagnosis and Early Warning Systems

Activity 1: This collaboration aims at developing in Italy a screening model for early detection, brief intervention and improved treatment for addictive disorders, especially among adolescents and young adults, through motivational counseling, professional drug testing and educational support to families according to the US Screening, Brief Intervention and Referral to Treatment (SBIRT) model.

Activity 2: A study of pharmacology and toxicology on new synthetic psychoactive molecules in animal model was activated with the Clinical Pharmacology and Therapeutics Research Branch, Chemistry and Drug Metabolism Section. The study aims at assessing acute, sub-acute and chronic toxicological effects brought about by New Psychoactive Substances in an experimental system checked and certified according to GLP (Good Laboratory Practices).

Activity 3: A study to evaluate the tolerability and efficacy of a ketogenic diet in the reduction of withdrawal symptoms in hospitalized alcohol-dependent subjects.

Activity 4: In the framework of the AIDS Research Program, a collaboration was activated in order to study the mutation of the HIV virus in a cohort of patients treated in an Italian therapeutic community so as to understand whether and how therapies can influence such variations in the course of time.

United Nations Interregional Crime and Justice Research Institute (UNICRI)



unicri
United Nations
Interregional Crime and Justice
Research Institute

Area of collaboration: Scientific collaboration

Activity: It is a collaboration for the implementation of initiatives aiming at promoting the scientific communication and the sharing of evidence-based information within the scientific community. This collaboration led to the creation of the Drug@News institutional website, the Italian Scientific Community on Addiction and the Italian Journal on Addiction.

Media Research Lab at Iowa State University, Department of Psychology, Ames, USA



Area of collaboration: Mass media effects on the health of children and adolescents

Activity: Research collaboration on the effects of the use of videogames on the psychology and behavior of young people in particular, on the effects of violence in TV programs, films and videogames on both peer relationship and behavior, and on the pathological computer use.

Friends Research Institute, Baltimore, USA



FRIENDS RESEARCH INSTITUTE

Area of collaboration: Outcome evaluation

Activity: This collaboration aims at drafting a scientific article on the electronic clinical data and service supply record system in health facilities devoted to the care and treatment of drug addicted patients. In particular, the electronic health record, in Italy represented by the multifunctional platform MFP, plays a very important role in opioid agonist treatment and allows to monitor and evaluate precisely and scientifically the patients' outcomes across treatment facilities (Addiction Departments).

NYU Child Study Center (CSC), New York, USA



Area of collaboration: Neuroimaging

Activity: Study on the correlation between behavioral disorders and substance use in adolescents and young adults. This collaboration consists in: the acquisition and exchange of data regarding MRI and spectroscopy sequences for the analysis of metabolites; recruiting patients so as to analyze fMRI "resting – state" signals; comparing groups of subjects affected by ADHD and groups of subjects with substance use in order to detect anomalies in both the grey and white brain matter. The study aims at both understanding biological and cognitive aspects of the brain from an anatomical and functional point of view in adolescents and young adults (aged 15-30) who use drugs, and at understanding how different substances can affect brain maturation and whether some behavioral social and organic factors can affect the natural trajectory of brain development.

University of Wisconsin, Brain Laboratory of Neuropsychology and Brain Imaging, Milwaukee, USA



Area of collaboration: Neuroimaging of addiction

Activity: Examination of the effects of marijuana, alcohol, nicotine and ecstasy on brain structure and function through the use of magnetic resonance imaging and neuropsychological assessment. This collaboration aims at outlining effective treatment methods for adolescents who make frequent use of drugs. Several advanced magnetic resonance techniques are employed in order to study the neurotoxic effects of different drugs on young subjects (aged 15-22).

The analysis on the correlation between the MRI anatomo-functional and anamnestic- toxicological data allow to define the variables (early starting date of use, type of the substance used, poly drug use, comorbidity with stressful events or other pathologies, family history, etc.) that can concur to the formation and/or retention of the drug use behavior.

University of Hertfordshire, School of Pharmacy, United Kingdom



Area of collaboration: Pharmacology

Activity: This ten-year long standing collaboration consists in keeping a constant updating of the pharmacological aspects related to New Psychoactive Substances. In particular, in the last 5 years a joint effort has been carried out for the exchange of technical-scientific information and the identification of both pharmacological properties and clinical-toxicological characteristics of New Psychoactive Substances.

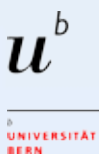
UC Irvine Child Development Center (CDC), Division of Developmental & Behavioral Pediatrics, Irvine School of Medicine, Irvine, USA



Area of collaboration: Neuroeducation

Activity: To disseminate at national level the scholastic intervention model for children with attention-deficit, learning-deficit and behavioral problems, promoted by the Irvine Child Development Center (CDC). This collaboration aims at developing and implementing such model also in the Italian context as a tool for detecting both vulnerability and risk factors for the use of substances and for developing preventative actions through the involvement of parents, teachers and educators.

University Hospital of Psychiatry, University Bern, Svizzera



Area of collaboration: Psychiatric Neurophysiology

Activity: Study of the physiopathological mechanisms of addiction observed by means of the Magnetic Resonance and the Arterial Spin Labeling techniques (ASL). The goal is to measure patients' cerebral blood flow and then compare results with control subjects.

University of Wisconsin, Madison, USA



Area of collaboration: Neuroimaging

Activity: The collaboration aims at the execution of a study on the brain development of both children and adolescents and on their predisposition to use drugs that could derive from the influence of genetic, epigenetic and environmental factors. The main goal of the research is to investigate on the cerebral circuits which are responsible for decision taking, motivation and addictive behavior in adolescents that have recently started to use drugs.

Ethical Consortium for young peoples health and the prevention of drug use and alcohol abuse

In collaborazione con



The Health Value



The health promotion process – which is meant as physical, mental and social wellbeing (OMA 1948) – is a value belonging to every society which want to protect its citizens from risks and dangers. Proper nutrition, healthy physical activity and good sleep could be considered protective factors of human health. All these factors can be transferred in a set of behaviors defining the quality of a person's health, thus acting on what is

called the "Health Value". If a person adopts negative behaviors, his/her whole health could be compromised. In particular, if a teenager – whose body and mind are still in a developmental phase – adopts behaviors such as drug use and alcohol abuse, he/she seriously endangers the quality of his/her health.

Ethical Consortium's national Network

- 75 adherent municipalities
- 93 testimonial



The Ethical Consortium



The Ethical Consortium is born to promote the "Health Value" between young and adult people endorsing healthy life styles, away from drug use and alcohol abuse. It aims at providing support to families, educators and teachers for a better growth of young people. It is a Community set up by authorities and opinion leaders who want to give testimony of the positive value of healthy and satisfying behaviors to help create an environment where citizens could live and preserve their physical, mental and social wellbeing.

Ethical Consortium's goals

Thanks to the collaboration agreement between the Italian Department for Antidrug Policy (DPA) of the Presidency of the Council of Ministers and the National Association of Italian Municipalities (ANCI) for the prevention of drug use and alcohol abuse, signed in Rome on December 18th 2012, it is possible for municipalities to join the Ethical Consortium in order:

- To communicate to young people – through a clear and explicit message from authorities and opinion leaders – the need and the opportunity not to use any type of drugs or alcohol, maintaining healthy lifestyles and behaviors.
- To prevent the use and the addiction to alcohol and drugs and, therefore, accidents and diseases drug and alcohol related.
- To promote the participation of positive opinion leaders within Italian Municipalities in the Ethical Consortium Ethics thanks to their endorsement of its principles against the use of all drugs and the alcohol abuse.

Ethical Consortium's principles

1. To maintain and demonstrate our ethical and professional commitment in the prevention of drug use and alcohol abuse.
2. To promote and strengthen the educational and preventive role and value of family, school and community, as reference points for health matters.
3. To contribute in promoting a multidimensional, challenging, creative, competitive social offers – in contrast with the drug market – to stimulate young people with healthy, fun and rewarding experiences. At the same time to increase their awareness and responsibility to prevent the use of drugs and the alcohol abuse.



4. To uphold children and adolescents' rights to be protected by drugs and alcohol provision and to grow in a healthy and drug-free environment.
5. To promote an awareness of the value and the "pleasure" of physical and mental health, of its protection and promotion.
6. To promote the practice of discovering and early detecting any drug use at a young age and behavioral conditions of vulnerability.
7. To consider addiction as a brain disease that can be prevented, treated and cured through proper treatment and never giving up the full social rehabilitation of drug addicts.
8. To promote scientific researches aimed at understanding the human brain's and the individual and social behaviors' operating principles, in order to define more effective interventions for prevention and treatment of addiction.

9. To promote and support the prevention and combat production, trafficking and drug-dealing by the side of the law enforcement agencies.
10. To contribute to the dissemination and application of the Ethical Consortium's principles.

Social disapproval of drug use

Communities themselves have to express a clear dissent against any behavior that would endanger people's health and have to disapprove social behaviors and values that support unhealthy or socially harmful lifestyles. The perception of being socially disapproved provides a strong deterrent to drug use and alcohol abuse, indeed. Keyes' studies (2011) show that the lower the disapproval of the use of marijuana in subjects when age increases, the greater the use of the substance. On the contrary, the greater the disapproval of marijuana use, the lower is substance use in adolescents, calculated over time.

Figure 1: The lower the disapproval of the use of marijuana in subjects when age increases, the greater the use of the substance. Keyes, K.M. et al. 2011.

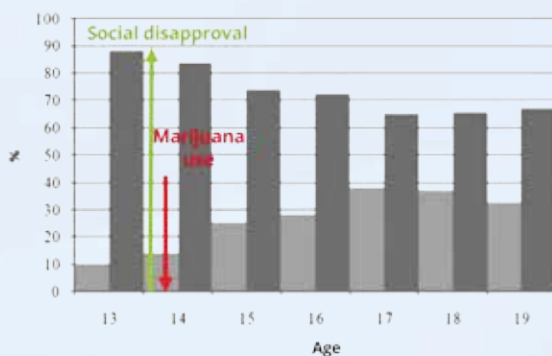
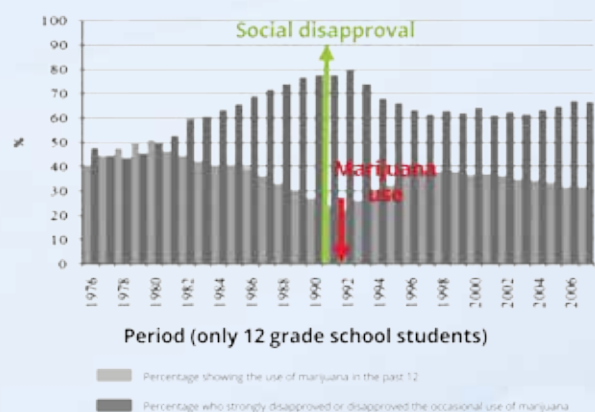
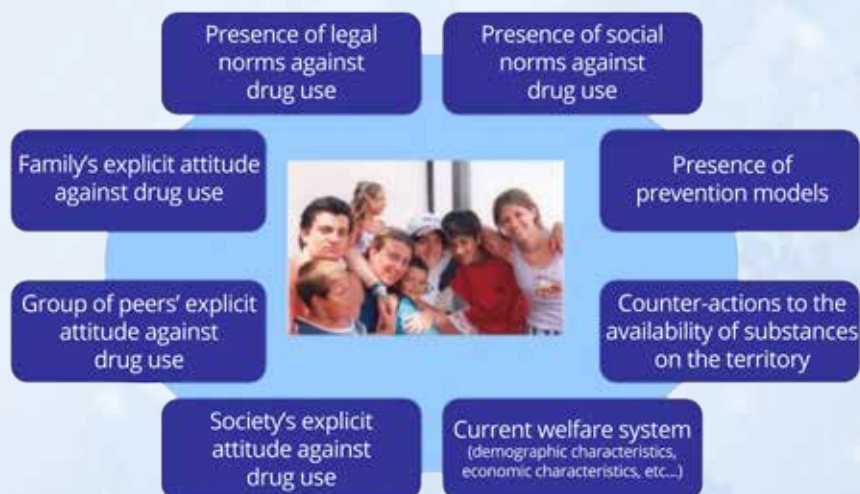


Figure 2: The greater the disapproval of marijuana use, the lower is substance use in adolescents, calculated over time. Keyes, K.M. et al. 2011.



Factors supporting social disapproval.



Early detection of drug use for early intervention among children



Serpelloni G.¹, Gomma M.², Rimondo C.¹, Zermiani M.²
¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri; ²Dipartimento delle Dipendenze - Azienda ULSS20 Verona; ³Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga, PCM

Delay time in identifying substance use

The perception of risks and damages resulting from the early use of drugs and/or psychotropic substances is often underestimated by both the young and their parents. This can result in a delay in the diagnosis of substance use and therefore in the continuation of a behavior able to cause very serious damage to mental and physical health of the young. Therefore, it is necessary that parents pose a particular attention to their children as early as in the pre-adolescent phase, in order to capture any signal of behavior at risky of drug use and to act promptly, with access to health care experts. According to the Annual Report to Parliament on the state of drug addiction in Italy 2011 the period between the age of onset of drug use and age at first treatment (delay time) varies between 5 and 9 years Depending on the substance, exposing the subject to high risks to their health.

Età di inizio	Primo trattamento	Delay time
Eroina: 21 anni	Eroina: 26 anni	5 anni
Cocaina: 22 anni	Cocaina: 31 anni	9 anni
Cannabis: 17 anni	Cannabis: 25 anni	8 anni

National guidelines

The manual aims to provide guidelines and methodological elements to operators of the Addiction department about strategies and techniques for early identification of behavioral risk factors for the development of addiction and the use of drugs among adolescents.

Link for download:

http://www.dronet.org/pubblicazioni_new/pubbl_det.php?id=663

Collaborazioni e patrocinii



<https://diagnosiprecoce.dronet.org/>

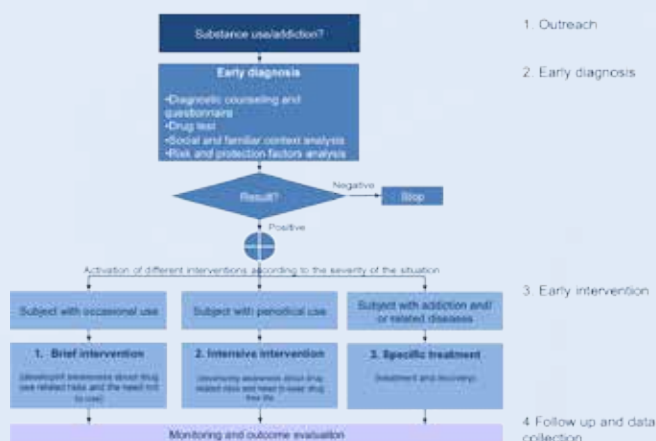


Institutional website on early detection of drug use

National information campaign



Operative framework



1. Outreach
2. Early diagnosis

3. Early intervention
4. Follow up and data collection

The "Early detection for early intervention among children" project

The project, initiated in 2012, aims to identify as early as possible minor subjects drug users and to activate as soon as possible adequate intervention measures. It involves operators of the Addiction Departments, parents, teachers and other educational figures.

Intervention area: 51 collaborating centers

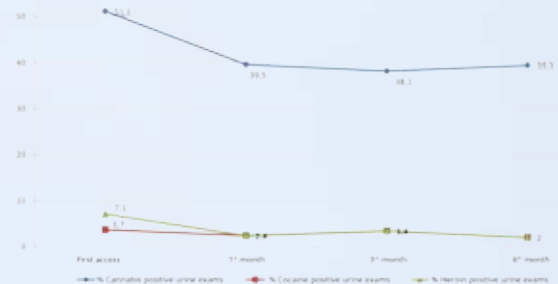
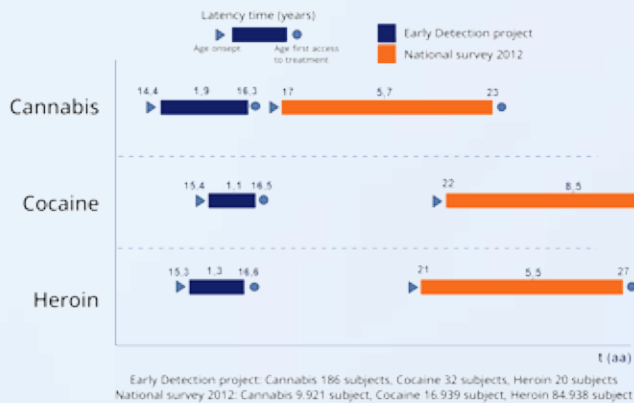


Main results (Mach 2014)

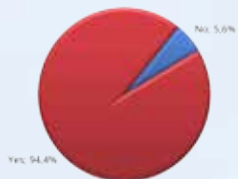
Through the project it was possible to record 297 young subjects attending health services implementing the model of early diagnosis and intervention proposed at national level (75.9% males and 24.1 females, mean age 14.4 years (min. 11, max. 17). The project also involved 523 parents (266 mothers and 257 fathers).

Delay time: elapsed time between the beginning of drug use and first contact with the services of diagnosis and treatment (measured by means of the Early Detection Project) compared with the times recorded in the absence of interventions for early detection at the Addiction Departments.

Subjects for substance use and percentage of positivity on the number of exams – Percentage



Use of substance



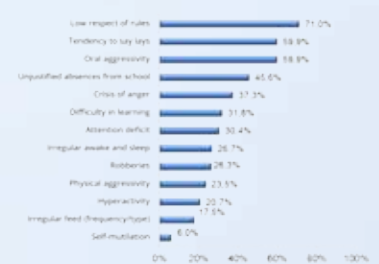
Behavioral disorders diagnosed



Behavioral disorders observed



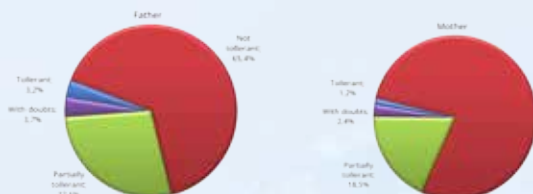
Type of observed disorder



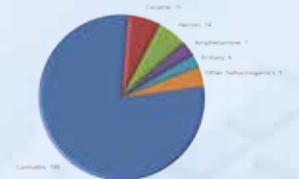
Micro-traffic



Attitude of parents toward use of illegal substances



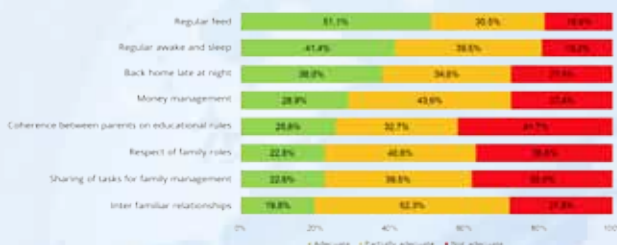
Numero soggetti per riferito uso di sostanza ultimi 30 giorni



Sexual behaviors at risk



Analysis of educational models

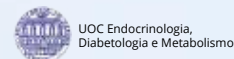
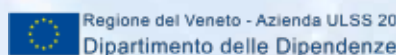


Conclusion

The model of diagnosis and early intervention so far achieved by the project "Early detection for early intervention among children" showed a significant reduction in the time between the onset substance use and the access to services (reduction of delay time); an ability to identify subjects with behavior of substance use (alcohol, tobacco, drugs) higher than that recorded from the National SPS, 2012, and a reduction in the consumption of substances also after 6 months of monitoring. In addition, it is important to highlight that the project has led to a real change in mentality, a cultural revolution among operators of services who have started to work in view of the early diagnosis and intervention with individuals much younger than usual patients and who have also been able to reorganize their internal resources to provide an adequate service to young people and their families.

Ketogenic diet: tolerability and efficacy in the reduction of withdrawal symptoms in hospitalized alcohol-dependent subjects

In collaboration with



Serpelloni G.¹, Volkow N.², Gomma M.³, Brunetto G.P.⁴, Corso F.⁵, Bonora E.¹, Zenti M.G.³, Seri C.¹, Rimondo C.³
¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri; ²Director, National Institute on Drug Abuse, USA; ³Dipartimento delle Dipendenze - Azienda ULSS 20, Verona; ⁴Medicina delle Dipendenze e Alcolologia di Marzana del Dipartimento delle Dipendenze ULSS 20, Verona; ⁵Divisione di Endocrinologia e Malattie del Metabolismo, Dipartimento di Medicina, Azienda Ospedaliera Universitaria Integrata, Verona

Background



The results of the PET study indicate that in fact, alcohol intoxication significantly reduces the overall brain glucose metabolism. In contrast, the alcoholic intoxication produces a significant increase in cerebral absorption of the tracer used. The study results also confirm a reduction in cerebral glucose metabolism during alcohol intoxication and document an increase in the brain uptake of acetate. The variations in the opposite direction between the decrease of glucose metabolism and the increased absorption of acetate in the brain support the hypothesis that during alcoholic intoxication the brain can count on acetate as an alternative source of energy and provides preliminary evidence that exposure to high amounts of alcohol would facilitate the use of acetate by the brain, as an energy substrate (Volkow et al., 2013). In addition, recent

findings with Magnetic Resonance imaging have shown that alcoholics promote metabolism acetate in the brain compared with control subjects, as consistent with the changes in energy use associated with chronic alcohol abuse (Jiang et al., 2013). These results raise the question of the potential therapeutic benefits that the increase of acetate concentration in plasma (which can be induced, for example, through a ketogenic diet) may have in alcoholics undergoing alcohol detoxification.



Aim of the study

The present study, exploratory in nature, has as main objective to evaluate the tolerability of the introduction of a ketogenic diet in patients hospitalized for the treatment of alcohol addiction, by collecting information on possible side effects of the diet and by evaluating its preliminary efficacy in terms of decreased withdrawal symptoms with or without the drug treatment in use at the hospital (benzodiazepines).

The study also aims to measure the degree of adherence of alcohol-dependent patients admitted to a ketogenic diet in place of a pharmacological treatment for withdrawal symptoms. Secondly, the study also intends to analyze information on metabolic and functional changes in the brain induced by the particular diet regimen, through the use of high field (3.0) Magnetic Resonance techniques (MR).

Principal inclusion criteria

- Men aged 18-65 years
- Individuals knowing the Italian language so as to understand and sign the informed consent.
- Subjects with alcohol problems who meet the diagnostic criteria for alcohol dependence according to DSM-IV-TR
- Subjects who declare that they have consumed alcohol at least once in the four weeks prior to assessment of eligibility and to the start of treatment.
- Subjects who express the desire to achieve abstinence or greatly reduce alcohol consumption
- Subjects that are in good medical conditions at clinical evaluation
- Subjects not in drug treatment for a disease included among the exclusion criteria
- Subjects with a standard body mass index (BMI < 29,9)
- Subjects with total cholesterol value less than or equal to 260 mg/dl



Principal exclusion criteria

- Subjects with benzodiazepine dependence, according to DSM-IV-TR
- Subjects that have a clinical history with serious neurological disorders: epilepsy, previous TIA / stroke or other vascular brain diseases found, Parkinson's disease, Huntington's disease, Multiple Sclerosis
- Subjects with unstable medical conditions
- Subjects with severe liver disease
- Subjects with diseases such as diabetes, heart disease, kidney deficiency, metabolic deficiencies, atherosclerosis, cancers, chronic pancreatitis
- Subjects with eating disorders
- Subjects with values of total cholesterol greater than 260 mg/dl
- Subjects with total cholesterol value less than or equal to 260 mg/dl, but which have two or more cardiovascular risk factors such as family history of heart attack, family history of myocardial infarction, thrombophilic disorders, family thrombophilic disorders, family history of high cholesterol, obesity
- Subjects with hypertriglyceridemia (greater than 200 mg/dl)

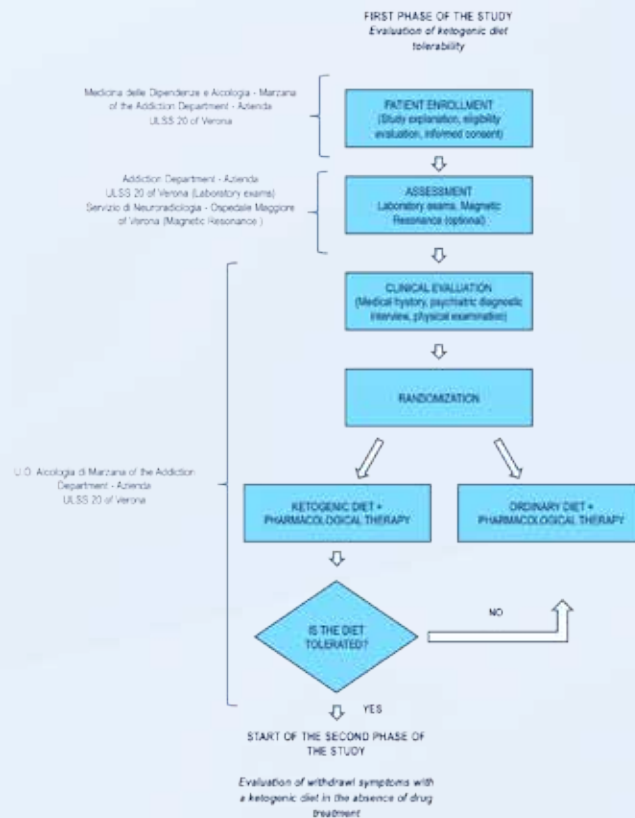
Experimental design of the study

The study will be carried out in two distinct sequential phases (sequential to one another).

First phase: to n alcoholic patients in treatment and the possible reduction of the doses of medication administered for the containment of withdrawal symptoms.

Second phase: to determine if the ketogenic diet reduces signs and symptoms of withdrawal in the absence of pharmacological treatment.

The following describes the sequence of activities planned:



Evaluation of the effectiveness of the diet

Primary outcome	Secondary outcome
<p>First phase of the study: Tolerability of the ketogenic diet assessed by monitoring the following parameters:</p> <ul style="list-style-type: none"> - Liking of the ketogenic diet by patients - Reduction of drug therapy administered for withdrawal symptoms (evaluated as a reduction of the number of doses of drug) - Reduction of the clinical withdrawal symptoms as measured by the assessment of the signs and symptoms according to the scale CIWA-Ar. 	<p>Reduction in the intensity of craving for alcohol.</p> <ul style="list-style-type: none"> • Absence of any alcohol consumption. • Metabolic and functional changes in the brain measured with MRI. • Changes in cortical excitability as measured by Transcranial Magnetic Stimulation.
<p>Second phase of the study: Reduction of the clinical withdrawal symptoms as measured by the assessment of the signs and symptoms according to the scale CIWA-Ar.</p>	

Expected results

It is expected to demonstrate the positive effects can be achieved with the ketogenic diet in the control of abstinence in alcoholics in treatment. The ability to define by MR the cerebral metabolic and functional structure will allow to define this type of food regiment as a possible additional therapeutic intervention in the context of alcohol addiction and at the same time to identify which areas and processes of the brain are involved.

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Prevention of drug and alcohol related road accidents

Drugs on Street protocol and NNIDAC project

D.O.S. Protocol

"Drugs on street" is a national protocol for the prevention of drug and alcohol related vehicle crashes, with the aim of investigating the prevalence of both psychoactive substances and alcohol in the general driving population (under artt. 186, 186bis, 187 of the Highway Code). The operating procedure is carried out jointly with the support of law-enforcement agencies and health care professionals. Toxicological tests are performed in order to investigate drivers' physical and psychic conditions possibly related to drug or alcohol use. The results of toxicological and clinical tests enable an assessment of driver's suitability to drive.

The activity is generally performed in the nighttime (24.00 – 6.00), during weekends. After breath alcohol tests are carried out by Law Enforcement on randomly selected drivers, they undergo clinical and toxicological tests performed by health professionals (medical history about drug use, screening drug test, clinical test, assessment of nervous responses, blood drawing for confirmation analysis).

Pictures of the phases in which the D.O.S. Protocol is articulated: police road control, breath alcohol test, reaction time test.



NNIDAC project



The Department of Antidrug Policies of the Presidency of the Council of Ministers has promoted the spread of the D.O.S. Protocol by means of a national network for the prevention of drug and alcohol related vehicle crashes (NNIDAC). The general aim of the NNIDAC project is to contrast the drugged and drunk driving phenomena by way of the creation of a national network applying standard procedures for road control. The NNIDAC project, which has existed since 2010, is currently active in 21 Italian municipalities.

Data collection method

A certification form, in triplicate, has been structured for a coherent data collection. The form is divided into fields that must be filled out by law enforcements officers (yellow coloured) and fields filled out by health professionals (grey coloured).

The first copy remains to the medical staff and it is stored in the driver's medical record for medico-legal purposes. The second one remains to the police officer who carried out the driver's road control. The third one, anonymous, is used for statistical purposes.

Partnership:



Ministero della Salute



NNIDAC web platform



A web platform has been designed for both data entering and consulting statistical files which synthesize results of the project activity. The web platform is accessible at the web address: <http://nnidac.dronet.org/>

Through the login, it is also possible to create and customize synthetic reports containing graphs, tabs and some indicators elaborated on the basis of the inserted information. All municipalities that have joined the project can access the platform.

Results of activity

The following preliminary results are referred to the activity carried out between July 2012 and December 2013. 97,4% of NNIDAC project's activity has been carried out outdoor, on the road. Drivers were controlled by local police (70,5%) and traffic police (14,7%). The type of vehicle more frequently inspected was the car (96,2%). Most of the drivers were tested for alcohol (76,4%), 22,8% were tested for both alcohol and drugs, 0,8% were tested for drugs only. 85,2% of drivers resulted negative for alcohol; 10,5% resulted positive for alcohol; 2% resulted positive for drugs; 2,3% resulted positive for both alcohol and drugs.

Among drivers who resulted positive for breath-test (15,7%), 18,7% had a blood alcohol concentration (BAC) between 0,5 - 0,8 g/l; 35,6% had a BAC between 0,8 - 1,5 g/l; 13,6% had a BAC higher than 1,5 g/l (punishable by means of vehicle confiscation); 29,1% had a BAC between 0 - 0,5 g/l, legal limit for drivers under 21 years of age, novice drivers and professional drivers.

Among drivers positive for saliva drug test, cannabis is the most frequently detected drug (39,7%), together with cocaine (22,4%) and amphetamines (6,9%). Some drivers tested positive for both cannabis and cocaine (15,5%). The urine drug test was made to verify drivers' substance use in the previous days (up to one week before). Results showed a frequent use of cannabis (53%), cocaine (25,2%) and a combined use of both cannabis and cocaine (14,8%).

Outcomes of the controls carried out among drivers tested for alcohol and drugs (2012-2013 data)



Informative tools for drug free schools



Serpelloni G.¹, Corradini M.G.², Rimondo C.³, Bevilacqua A.⁴, Brunetto M.⁴, De Liso R.⁵, Candio D.⁶
¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri; ²Ministero dell'Istruzione, dell'Università e della Ricerca; ³Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga, PCM;
⁴European Institute for Health Promotion; ⁵Dipartimento delle Dipendenze, Azienda ULSS20 - Verona

Prevention in school with video conferencing

National and international experts working in the addiction field by different agencies all around the world are available to share their knowledge and expertise with Italian students on the topic of prevention of drug use and alcohol abuse. This is possible through the sophisticated technology of EDULife videoconferencing, which connects simultaneously renowned experts with many Italian schools, at no cost to the participating educational institution.



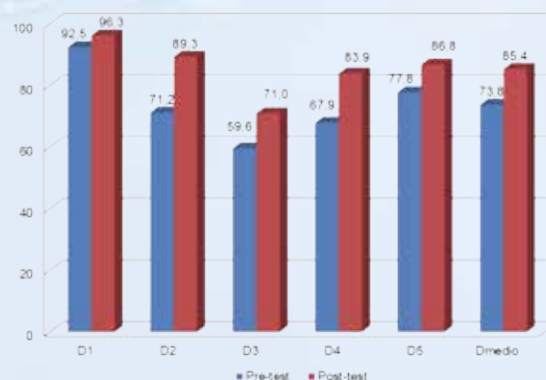
Output indicators 2011-2014

- 7093 participating students
- 19 Italian Regions
- 102 schools involved
- 55 videoconferences



School year 2013-2014 (preliminary results)

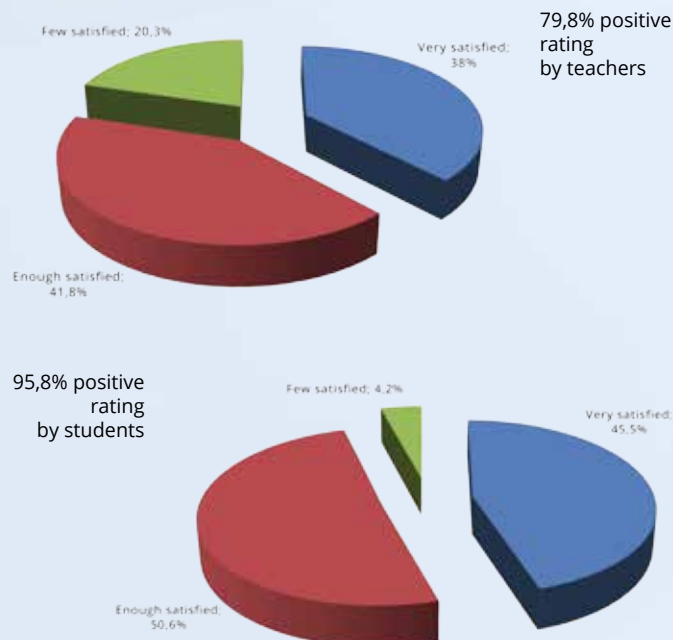
Learning assessment



- D1 - "What are drugs?"
 D2 - "Could the use of drug change the brain?"
 D3 - "Which effects may cause cannabis use?"
 D4 - "Could alcohol be considered a drug?"
 D5 - "Is smoking cigarettes addictive?"

Average learning increase: +11,6%

Satisfaction evaluation



EDU platform

Educational operating system (<http://piattaformaedu.dronet.org>) addressed to teachers and parents, which can be accessed online free of charge, upon registration. On the platform many training courses on drug use and alcohol abuse are available. They could be used both at school or at home. Thanks to the dedicated forum which facilitates debates, it is also possible to interact with other users. The new service "Sportello Scuola" (sportelloscuola@dronet.org) is dedicated to educational professionals who need to find answers to specific doubts and questions arisen from their daily activities with students.



"Are you against drugs and the mafia" initiative



Initiative aimed at making aware young people on the risks of drug use, alcohol abuse, mafia and related violence and terrorism through the implementation of creative activities which can lead to new ideas and incentives. Creativity could be indeed a source of pleasure and can support and inspire young people by enhancing their motivation to express their potential and to maintain healthy lifestyles, in full compliance with the law. The "Ci stai contro le droghe e le mafie?" initiative is addressed to students attending Italian first and second grade high schools. They should realize posters, banners and website homepages addressed to young people endorsing an explicit message against drug use, alcohol abuse and mafia. Procedures and materials are available at the website <http://www.cistaicontrolledroghe.dronet.org/>

- 33 subscribed schools
- 246 participant students
- 105 creative products arrived

Gambling

Serpelloni G. - Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri

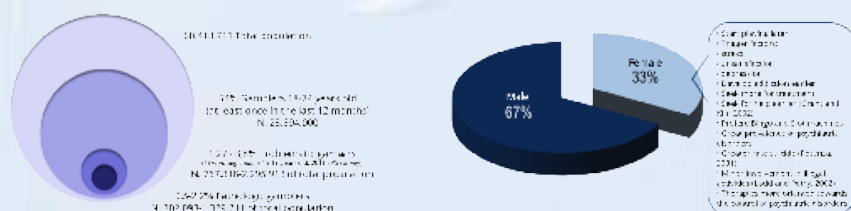
Definitions

Gambling consists of betting money, or other valuable goods, in order to obtain a prize, on an event the outcome of which, in whole or in part, is determined by chance. Pathological gambling (GAP) is a morbid form clearly identified, that in the absence of appropriate measures of information and prevention, may represent a real social disease. The GAP is still a disease preventable, treatable and curable, which requires early diagnosis, specialist care and psychological and social support. A more extensive definition of pathological gambling is available in the DSM-5.

Stages of Gambling

Informal and recreational gamble	Physiological behavior with the need of awareness for the potential risks	Characteristics
Problematic gamble	Conduct at risk for health (physical, mental and social) with the need for diagnosis and early intervention	- Occasional game - Main reason: socialization and competition - Expenditure contained
Pathological gamble	Neuro-psycho-biological disease with health and social consequences and need for diagnosis, treatment and rehabilitation	- Periodic game - Increased time spent playing - Increase in expenses dedicated to the game - Daily or intensive play - Craving (uncontrollable desire to play) - Charges with high debt

Il gioco d'azzardo in Italia: dati epidemiologici

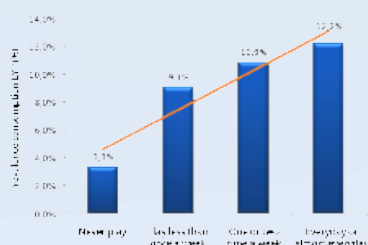


Fonte: Ministero della Salute, 2012.

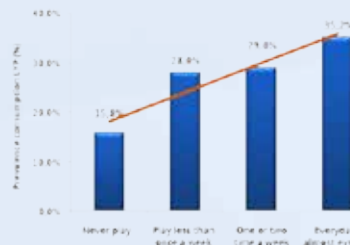
Subjects in treatment

In 2011, a survey was conducted by the Department of Antidrug Policies, which involved Italian Regions and Autonomous Provinces Italian and that allowed to partially detect a proportion of subjects treated at Addiction Departments/Ser.D. Emilia-Romagna, Tuscany, Basilicata, Sardinia, Umbria, Valle d'Aosta and the Marches did not take part to the research. The sample, though partial, is however interesting and consists of 4,544 subjects, of which 82% males and 18% females.

Consumers prevalence % of any illegal substance (use last 12 months) by type of player - General population 18-64 years. GPS-DPA 2012



Consumers prevalence % of any illegal substance (use last 12 months) by type of player - School population aged 15-19 years. SPS-DPA 2012

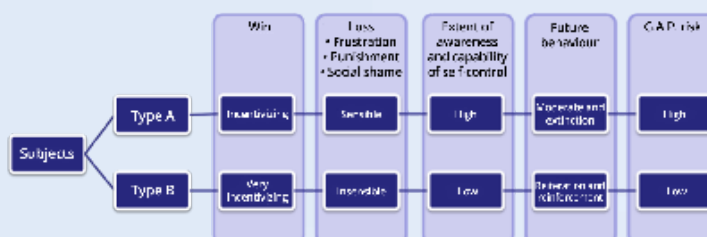


Consequences of pathological gambling

The pathological gambling can have a serious impact on the physical, mental, emotional, and financial condition of people who play, as well as on their families. The stress caused by gambling can cause physical and emotional problems such as anxiety, insomnia, depression, guilt, anger, and so on. It is not infrequent the recourse to the use of alcohol and drugs. Regarding economic aspects, debts can be substantial and, in some cases, it may happen that there is recourse to moneylenders. In the worst case, the situation can become so unbearable as to cause suicidal intent in the player in debt.

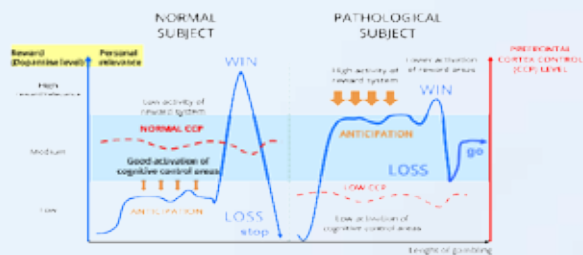
Resilience and vulnerability factors

Not all individuals who gamble develop a pathological form of addiction. There are differences in the population exposed to the game involving the existence of individuals more vulnerable than others to develop addiction (that is, pathological gambling), by virtue of individual, environmental and other factors, according to characteristics of the games. Depending on the personal vulnerability, behavioral paths that people can take when they are in contact and stimulated by means of gambling are reported in the following figure (Serpelloni, 2012).



Neurobiological aspects of pathological gambling

Subjects with pathological gambling perceive and appreciate the most, in terms of gratification produced, stimuli arising from gambling rather than the normal population. That is related to different structure of their dopaminergic systems and processes of gratification. Therefore, they tend to select and to reiterate the use of these stimuli rather than the other normal gratification stimuli. If you associate this dysfunction with other dysfunctions at neurocognitive level, such as control disorders (impulsivity and compulsivity), difficulties in problem analysis and problem solving, poor cognitive flexibility and the presence of irrational beliefs, the result is a complex but coherent framework of symptoms that explains the behavior of patients with pathological gambling.



GAP: subjects: greater reward in anticipation, lower reward after win, low CCP
Normal subjects: lower reward in anticipation, greater reward after win, normal CCP

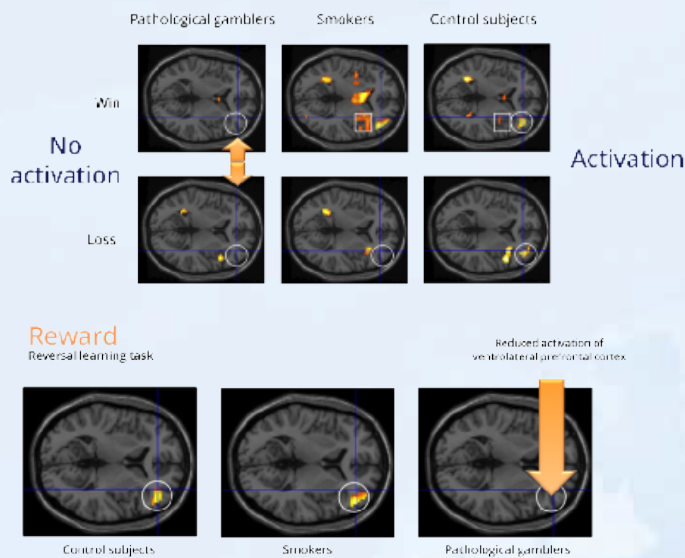
Some authors (Petry 1999, Clark 2009) found that in pathological gamblers, as well as in substance dependence, there is a more rapid resolution of satisfaction reward compared to non-vulnerable population. At the same time, there is a high reduction in the duration of the satisfaction derived from the rewards. This would explain the subsequent search for new and immediately repeated stimuli in pathological gamblers.

Functional MRI studies (Clark et al., 2009) have shown that in patients with pathological gambling, while the expectation of winning, an increased activity of the reward system is registered. After winning, in the areas of gratification there is an activity lower compared to normal subjects. During the game, a lower activation of the areas of control.

Gambling and neuroimaging

Research performed by means of advanced neuroimaging techniques in pathological gamblers showed a failure to activate the right ventrolateral prefrontal cortex (VLPFC), both in condition of monetary gain and of monetary loss (De Ruiter et al., 2009).

Other researches have also showed in problematic gamblers an activation of the VLPFC significantly poorer than smokers and controls (Remijne, 2006).

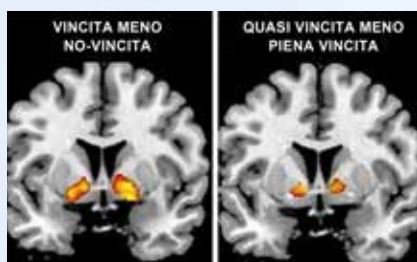


Investigations available in the scientific literature show that brain areas with greater response to images linked to gambling in pathological gamblers are regions involved in motivation and in visual processing, similar to the neural mechanisms underlying responsiveness to stimuli related to drugs in drug addiction.

Activation patterns between groups for images related to gambling compared to neutral images (Goudriaan et al., 2010).

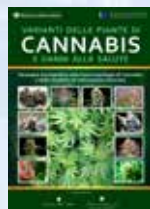


Activation of the insula in the case of near-win and real-win in pathological gamblers (Billieux J et al., 2012).



It was also shown that the "near wins" strengthen the desire to gamble by an abnormal involvement of the reward circuit, despite the objective lack of monetary reinforcement in these tests (Clark 2009). Subsequent studies (Billieux et al., 2012) have also shown that in gambling players, reactions of the brain areas of learning are almost equal when they win or near-win. That means that, in pathological gamblers, near win produces the same gratification as real wins do.

National guidelines and scientific handbooks



Variants of cannabis plants and health damage

March 2014

Author: Serpelloni G.

This iconographic manual has been prepared to provide an overview of the various and new types of cannabis seeds produced in the world. It is intended to provide a useful tool for all professionals who wish to deepen their interest or knowledge on cannabis seeds and the plants that they generate.



Gambling. A Self-Help Guide. Handbook for people with gambling addiction

March 2014

Authors: Serpelloni G., Gomma M., Rimondo C., Rossi A., Tito R.

The document is intended to be an important starting point for the person suffering from pathological gambling, a moment of reflection and awareness of the problems associated with gaming and the need to stop these dynamics.



G.A.P. National Action Plan 2013-2015

December 2013

Authors: Serpelloni G., Department for Antidrug Policies, Presidency of the Council of Ministers

The need for national guidelines on pathological gambling, in addition to meeting the requirements of the legislation, also comes from the real need to put in place as soon as possible, really effective preventive interventions to combat the phenomenon that have assumed relevance

and social and health importance.



NEW DRUGS. Update and National Action Plan for the prevention of the spread of New Psychoactive Substances (NPS) and the offer on the internet

Novembre 2013

A cura di: Serpelloni G., Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri

First and concise update on the main characteristics of the NPS identified, developing a series of strategic directions, objectives and actions to be able to start building an integrated and coordinated response between all administrations and organizations involved in various capacities, in order to cope this emerging problem.



New Psychoactive Substances (NPS): data sheets for the molecules recorded by the National Early Warning System

November 2013

Authors: Serpelloni G., Macchia T., Locatelli C., Rimondo C., Seri C.

NPS data sheets elaborated by the National Early Warning System which report information that can be of great benefit to professionals (laboratory personnel, personnel

of the emergency unit, healthcare professionals, researchers, etc.) in order to facilitate the analysis of unknown samples.



Report SPS-DPA 2012

October 2013

Authors: Serpelloni G., Simeoni E., Genetti B., Mollica B.

Report of the survey conducted on the student population aged 15-19 years in Italy with respect to the use of drugs. Database 2012.



Report GPS-DPA 2012

October 2013

Authors: Serpelloni G., Simeoni E., Genetti B., Mollica B.

Report of the survey conducted on the general population aged 18-64 years in Italy with respect to the use of drugs. Database 2012.



Drug use and related infectious diseases

October 2013

Authors: Serpelloni G., Cruciani M.

Drug use and dependence have always been associated with a variety of infections. While remaining the parenteral route of absolute importance, is to underline how the use of substances determine an increasingly important impact on risk behaviors such as sexual promiscuity, which in turn is an important cause of acquiring infections, HIV in first place.



Prevention of drug use and alcohol abuse - Collaboration Agreement DPA-ANCI

October 2013

Authors: Serpelloni G., Department for Antidrug Policies, Presidency of the Council of Ministers in collaboration with ANCI

Adhesion to the ethical consortium for the prevention of drug use and alcohol abuse through the activation of a network of Italian municipalities.



Annual Report to Parliament 2013

June 2013

Author: Serpelloni G.

National report on drug use and addiction in Italy. Data base 2012.



Problematic and pathological gambling: general overview, pathophysiological mechanisms, vulnerability, scientific evidence for prevention, treatment and rehabilitation

February 2013

Author: Serpelloni G.

This publication is directed to professionals of the Addiction Departments and wants to make a contribution to focus on the problem of pathological gambling on the basis of the scientific evidence with a multidisciplinary approach that highlight neurobiological, psycho-behavioral, social and financial aspects that are the basis of this phenomenon.



Prevention of drug use and alcohol abuse. Memorandum of Understanding MIUR-DPA

December 2012

Authors: Serpelloni G., Department for Antidrug Policies, Presidency of the Council of Ministers in collaboration with the Minister of Education, University and Research



Neuroscience of Addiction: Neuroimaging

November 2012

Authors: Serpelloni G., Alessandrini F., Zoccatelli G., Rimondo C.

The Department for Antidrug Policies, in collaboration with NIDA, the UNODC and the Department of Addiction ULSS 20 - Verona, has published this guide with the aim of offering to professionals working in the addiction field and to researchers working in academia, scientific information

on the role of neuroimaging of addiction in the clinical diagnostic practice and what possible prospects such evidence may result in the treatment of addictions.



RELI - Theoretical and Practical Handbook

April 2012

Authors: Serpelloni G., Frighetto R., Dalla Chiara C.

This manual defines the general guidelines and an operational model for the processes of social and occupational rehabilitation and reintegration of drug addicts and is addressed to all operators of the Departments of Addiction.



Early Detection and Early Intervention

November 2011

Authors: Serpelloni G., Gomma M., Rimondo C.

This manual aims to provide guidelines and methodological elements to the Addiction Department operators on strategies and techniques of early identification of behavioral risk factors for the development of addiction and drug use in adolescents. Is in fact recognized the

effectiveness of an intervention of this kind in interrupting the evolution of vulnerable people towards forms of addiction to substances such as heroin, cocaine or amphetamines.



The Department of Addiction. Guidelines and organizational orientations for the integration of supply and services

November 2011

Authors: Serpelloni G., Mollica R., Rimondo C.

In view of the great need to have precise methodological guidelines within the organization of Addiction Departments, the Department for Antidrug Policies has

developed this document which is intended to be a technical and scientific point of reference for improvement in the field of addiction.



General principles of the Italian position against drug use

November 2011

Author: Department for Antidrug Policies

This publication lists a summary of the basic principles of the Italian position against drugs.



The reasons why NO to the legalization of drugs

November 2011

Author: Department for Antidrug Policies

This publication analyzes the main reasons why it is believed that the legalization of the use of drugs is not an acceptable nor viable choice in our country to reduce the consumption of substances and reduce the problems related to their use.



Prison and Drugs

November 2011

Authors: Serpelloni G., Mollica R., De Luca C., Condemi M.

The main problems that have been willing to deal with this publication are those of the great heterogeneity that currently exists in making the diagnosis of "drug dependence", the cumbersome procedures used to quickly insert people into alternative measures, the lack of

coordination with the judiciary surveillance and ultimately the low percentage of eligible persons who enjoy today the benefits provided by art. 94.



Operating Manual SIND - National Information System on Dependencies

May 2011

Authors: Department for Antidrug Policies and Ministry of Health

This manual is a joint effort made by the central government, regional administrations and autonomous provinces, in order to have a common tool, agreed and well-structured to allow for a standardized data collection

and post-processing, which can ensure a good representation of the phenomenon.



Guidelines. Screening and early diagnosis of major infectious diseases related to substance use

January 2011

Authors: Department for Antidrug Policies and Ministry of Health

For several years it was found a significant decrease in the supply of HIV and hepatitis B and C tests, which could result in a substantial decrease delay in early diagnosis with respect to such infections, even with a reduction in access to antiretroviral therapies. Accordingly, this

document provides some guidelines based on a series of epidemiological surveys that have highlighted the need for urgent action to increase access to testing for HIV and hepatitis.



Cannabis and health damage

January 2011

Authors: Serpelloni G., Diana M., Gomma M., Rimondo C.

The publication focuses on a series of scientific information on the effects of cannabis and its derivatives to be offered to all operators in the sector and those people who want to realize how this kind of substance may be hazardous to the health. In the conduct of publication were examined issues

related to neuroscience but also to behavioral psychology and sociology.



National Action Plan (NAP) on Drugs

October 2010

Author: Department for Antidrug Policies, Presidency of the Council of Ministers

National Action Plan (NAP) on Drugs (which originates and is inspired by the EU Action Plan on combating Drugs 2009-2012) has been prepared referring to findings reported in the "Summary of the views expressed by operators in the

V National Conference on Drug Policy". This document provides an important starting point to be taken into consideration to outline a new plan that meets the emerging needs, identified in this meeting of institutional shareholders, as provided for by Presidential Decree 309/90 and subsequent amendments in the field of drug addiction.

Web monitoring Prevention of online drug sales and illegal rave parties

In collaborazione con

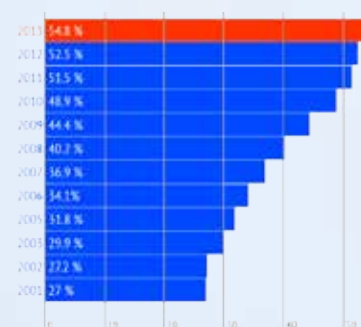
Serpelloni G.¹, Rimondo C.², Brunetto M.², Valvo G.²¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri; ²Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri

Drug and Internet

Internet gives the opportunity to access quickly and easily to a wide number of information, to be able to communicate in real time with the world and to start a commercial relations for any kind of product, including unfortunately, drugs. Internet is also a tool in which became possible to organize illegal rave party and access to the darknet, a new channel for illegal trade.

In the last 13 years, in Italy, the Internet users increased: from 27% (2011) to 54.8% (2013) – (Source: Istat Noi Italia 2014).

In this context, the Department for Antidrug Policies has activated a web monitoring unit, within the National Early Warning System which operates with the aim to identify and to obtain information on these phenomena and to prevent that users purchase and consume the substances sold on the web and the darknet. These illegal substances are often dealt during rave parties, which are notified by the web monitoring unit to the law enforcement, to prevent or to manage them, through their intervention.



The procedure to purchase drugs on the web



Darknet

The web contents that are not part of the Surface Web, which is indexed by standard search engines such as Google or Yahoo, are identified as Deep Web. Web monitoring unit has focused on identification of web sites dedicated to trade and promotion of illegal substances in the deep web. Furthermore, the web monitoring unit has identified sites of e-commerce for the sale of different products as seeds or plants of cannabis, drugs, homicides, weapons, deletion of criminal record.

Sites for killings

Sites for illegal market

Sites for drugs sale



Methods

The methods are based on research of websites in Italian language or with server located in Italy, easily accessible to any user interested to purchase illicit drugs. The procedure allowed the web monitoring unit has identified different types of psychoactive substances that are included in Tables of D.P.R. 309/90 and s.m.i., prescription drugs were identified as well. By the web monitoring unit, the National Early Warning System notifies the sites that commercialize illegal substances within standardized procedures shared with the Central Directorate for Anti-drug Services, Carabinieri N.A.S., Police, Prefectures, Municipalities. The procedures include:



Web sites

1. Identify and analyze the contents on the web sites of potential suppliers that freely commercialize psychoactive substances;
2. preparation of a report on information collected;
3. forward the report to the appropriate law enforcement authorities;
4. verify the outcome of sent report and update of recorded data on the monitoring activity.



Rave parties

1. Thematic research on the specialized sites;
2. preparation of technical report and document with information of the illegal event identified;
3. transmission of report to the competent authorities to initiate investigations of the case and communicate the result to the Department for Antidrug Policies.



Darknet

1. Browse on the darknet through directory of links to other sites (e.g. Evil Wiki, HiddenWikki, Torlink);
2. identify blog and forum to interact with users, to obtain useful information for monitoring activities;
3. notifying the intercepted sites to the appropriate law enforcement authorities.

Results

From July 2011 to April 2014, 541 web pages selling New Psychoactive Substances (NPS) were notified to the law enforcement, specifically to Carabinieri N.A.S.

Commercial site



Free advertisement boards on online marketplace

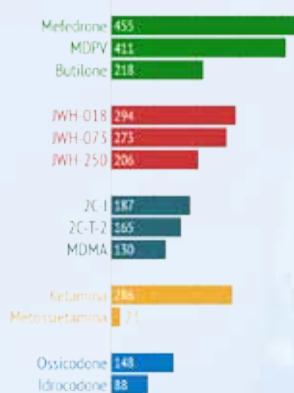
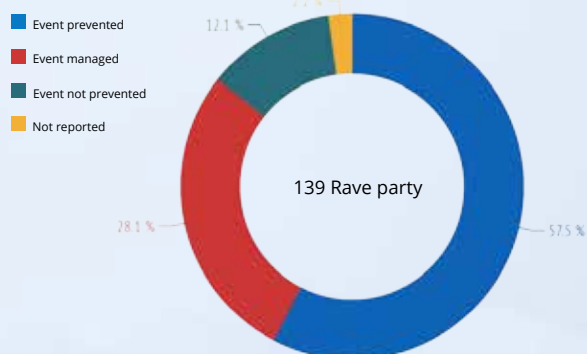
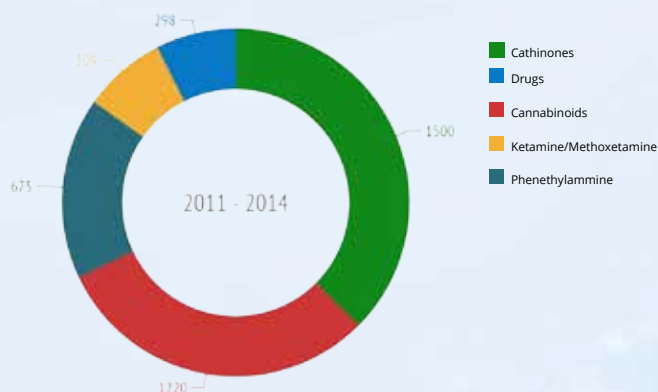


Social network / Blog

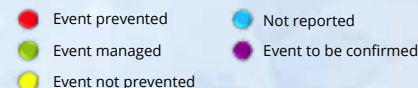


From October 2010 to April 2014, 139 illegal music events promoted online, were recorded (in Italy). These events were notified to the Prefecture, Police, municipality and referred to the Magistrate of the place where the event was to be held and the Central Executive for Anti-Drug Services, in order to verify the legitimacy of the organization.

Major structural groups and substances included in Tables of DPR 309/90 and s.m.i., identified from the web monitoring unit. Source: National Early Warning System, 2013.



Geolocation of reported rave parties by the Drug Control Policies Department and related outcomes



Functional, metabolic and cerebral blood perfusion abnormalities in drug addiction

Serpelloni G.¹, Alessandrini F.², Zoccatelli G.², Rimondo C.³, Bellamoli E.⁴

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Introduction



Magnetic Resonance Imaging (MRI) techniques have given strong impulse to the comprehension of the biological substrates of addiction. In particular alterations of functional connectivity, metabolism and blood flow perfusion could represented neural substrates of cognitive impairment in executive and general cognitive functions in drugs users. Such abnormalities has been suggested as a neuronal mechanism for the dependence and relapses in addiction.

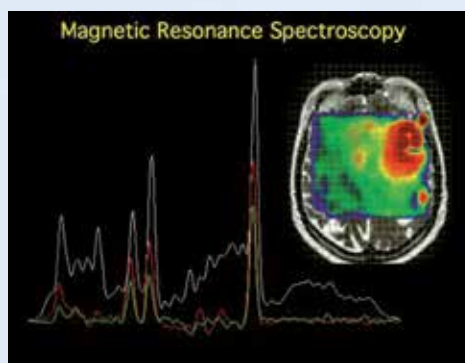
Methods

Functional Magnetic Resonance Imaging (fMRI) studies the neural activity in the brain. It shows which structures are active during particular mental operations, thus allowing the investigation of the neural networks activated by specific brain functions. We used fMRI tasks based on blood oxygenation level dependent (BOLD) method, which measure regional cerebral hemodynamic in order to make inferences about neural activity, indirectly.

Figure of the paradigm used



Magnetic Resonance Spectroscopy (MRS) measures brain biochemistry, which is the spatial distribution of metabolite concentrations and their combination both in white matter and gray matter tissue. We investigated the ratio and distribution of metabolites as Glx/Cr, Cho/NAA and Ins/Cr on 28 young cannabis users (mean age = 18y) compared to a healthy group.

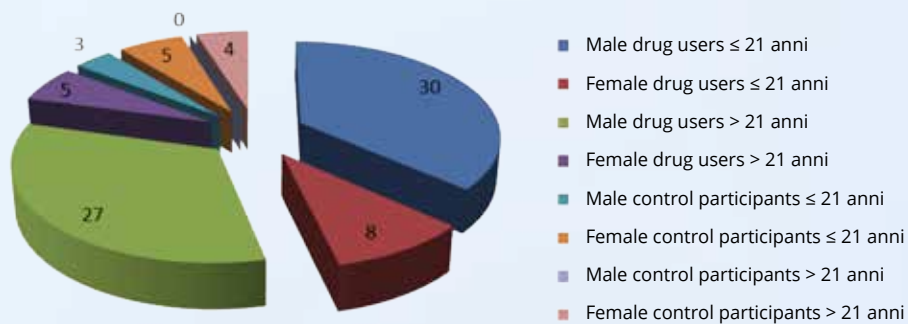


Continuous Arterial Spin Labeling (cASL) is a non invasive MRI method to study the cerebral perfusion without contrast media administration. cASL relieved the changes of cerebral blood flow (CBF) and allows to obtain maps of blood flow perfusion. We tested the differences in regional CBF of 10 cocaine users compared with 10 healthy controls and the gray matter density. We compared the CBF maps with the total intracranial volume (TIV) to rule out which brain areas shows abnormal perfusion and atrophy.

Preliminary analysis and results

Subjects underwent MRI

To date, 82 subjects (70 drug users and 12 controls) have been scanned in UO of Neuroradiology (Verona). Recruitment is still ongoing.



fMRI data

Subjects subdivision in "responder" and "no responder" depended of the time of abstinence (responder > 4 weeks). During craving, "no responder" subjects activated occipital cortex, thalamic nuclei and right frontal cortex. During resisting, the same subjects activated anterior cingulate and orbitofrontal cortex. "Responder" subjects, during craving activated early the left dorsolateral prefrontal cortex and orbitofrontal cortex. These early prefrontal activations may reflect stronger cognitive strategies of craving control in "responder" patients.

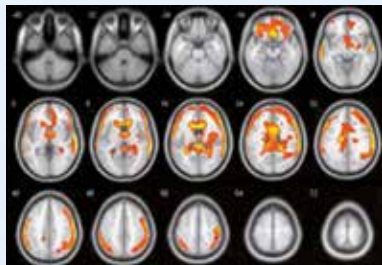
MRS data

Anterior and posterior cingulate have been chosen as ROI positioning MRS sequences (CSI) with TE=80/135/30ms. Cannabis users had Glx/Cr, Cho/NAA, Ins/Cr concentration levels out of the range. Data analysis relieved a reduced Glutamate (Glx) in ACC as altered rewarding mechanism, altered decision making and impaired of dopaminergic metabolism. We found also an increased Cho (turnover of membrane), a metabolic pattern similar to depressive syndrome. MRS data correlated with personality traits (novelty seeking).

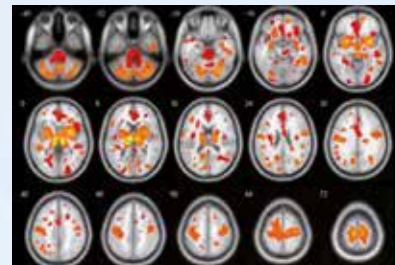
cASL data

Cocaine users showed an increased CBF in frontal gray and white matter deep areas (thalamus, basal ganglia), in temporal and parietal cortex. These subjects showed also a reduction of the gray matter density in deep areas (i.e, thalamus), parietal and frontal cortex.

CASL: cerebral hyperperfusion in cocaine users



Areas of reduced gray matter density in 10 cocaine users



Conclusions and future directions

Here in we have summarized some preliminary data of the project. Specifically, we have shown the presence of abnormal level of metabolites (Glx, Cho) in the cingulate cortex and abnormal cerebral perfusion in drugs users. Future analyses will be performed to confirm these observations. The data indicate in cannabis users a metabolic cerebral pattern like depression that correlates with specific temperament and character traits. Longitudinal analyses, along with the comparison between drug users and matched healthy controls, will be performed to evaluate morpho-functional and biochemical measures over time and to detect potential effects of medication, chronicity and age.

Evaluation of cortical thickness and white matter alterations in adolescent drug users with 3.0 T mri

Serpelloni G.¹, Alessandrini F.², Zoccatelli G.³, Rimondo C.³, Bellamoli E.⁴

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Introduction

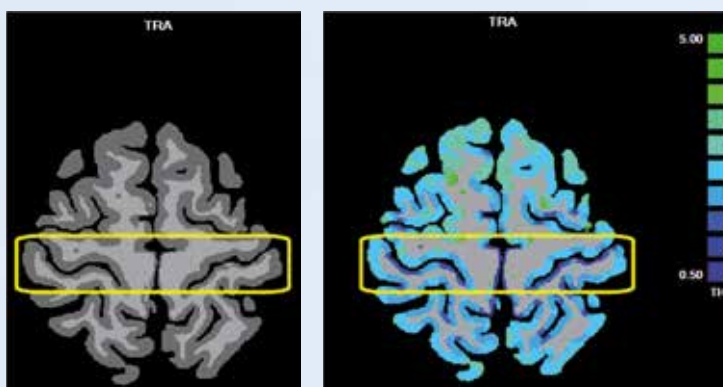
Cortical atrophy and alterations of inter-hemispheric white matter fibers connections has been suggested as a neural substrate of cognitive impairment in executive functions, language and general cognitive functioning in addictions. We assessed teen drugs users enrolled in the MRI project with a multimodal MRI and a full neuropsychological assessment to evaluate the brain and cognitive abnormalities after drugs consumption in adolescence population in comparison with a control group. MRI scans were performed in the Verona's University Hospital, Unit of Neuroradiology, with an high-field MR scanner. We aim to detect structural and microstructural abnormalities in adolescents affected by drugs addiction compared to healthy controls, utilizing the Cortical Thickness Analysis (CTA) and Diffusion Tensor Imaging techniques (DTI).



Methods

Cortical Thickness Analysis (CTA) is a non-invasive MRI technique that allows the quantification of neural tissue in terms of thickness of cortex. It is a process that permits to obtained morphometric informations about the cerebral gray matter. The procedure is based on measurements of brain cortical thickness of individual segmented cortical hemispheres. We compared 3D-T1 weighted images of 6 adolescent cannabis users (mean years = 16 y) with 6 healthy subjects.

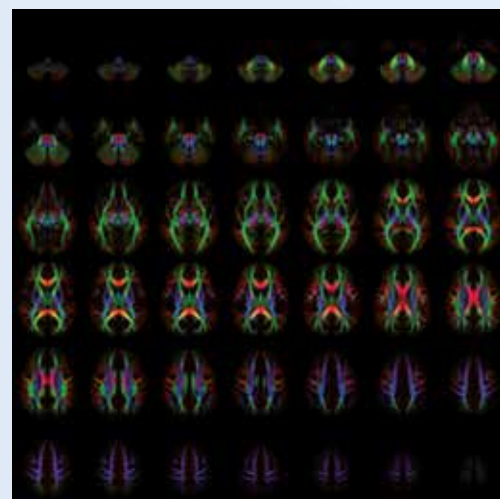
On the left, the cross section of the 3D-reconstruction of the cerebral hemispheres according to gray scale. On the right, overlay of the map of CTA colorimetric-based (TH). In the box, a detail of the motor cortex.



Diffusion Tensor Imaging (DTI) is a non-invasive MRI technique that allows the in vivo quantification of water diffusion through indices, which reflect the microstructural characteristics of the underlying tissues (Fig.3). The most common of these indices is fractional anisotropy (FA), which measures the preferential directionality of diffusion and mean diffusivity (MD) which it is an index of water diffusivity.

Tract-based spatial statistics allows the investigation of the possible differences in white matter (WM) tracts diffusion properties between groups of patients and healthy controls.

Axial scans of DTI maps using multidimensional vector algorithms based on 30 directions of the gradients. The DTI can be used to infer the connectivity of the white matter of the brain (tractography).



Preliminary analysis and results

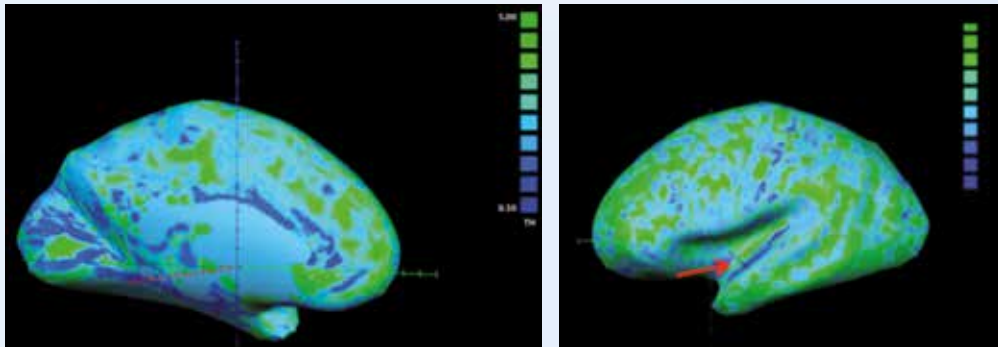
Subjects underwent MRI

To date, 18 subjects (9 drug users and 9 controls) have been scanned in UO of Neuroradiology (Verona). Recruitment is still ongoing.

CTA data

Post-processing analysis of data give us cortical thickness maps with areas of brain atrophy related to drugs addiction and cognitive impairments. We performed a computation of average thickness maps across subjects and statistic group difference maps obtaining a reduction of the cortical thickness in temporo-mesial areas and anterior cingulate cortex (blue, Figure 4a and 4b). Cannabis users showed a correlation between brain atrophy and deficit in neuropsychologic tests (impairment of attention and memory).

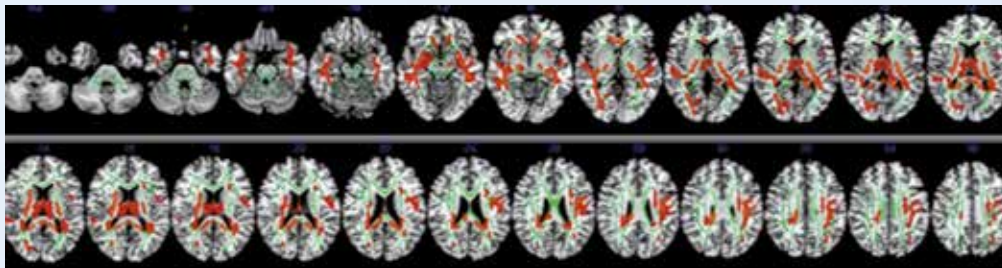
Results of CTA on 6 subjects affected by cannabis addictions versus 6 healthy controls. Blue areas indicate the thinner cortical thickness (atrophy) in temporal-mesial and cingulate cortex (left hemisphere).



DTI data

The TBSS procedure includes the following steps: 1) registration of the individual FA images to a common template; 2) creation of a skeleton of white matter tracts by thinning of the FA maps; 3) projection of individual FA values into the skeleton; 4) investigation of statistical difference between patients and controls. TBSS results in clusters of voxels that differ in the value of FA for healthy controls and patients, after correction for multiple comparisons. With this approach we obtained promising results when subjects affected by drugs consumption have been compared to healthy controls: differences in FA have been found in several regions, and more prominently in DPLFc, frontal and temporal areas, sub-cortical nuclei

Results of TBSS analysis for 9 subjects affected by cannabis addictions versus 7 healthy controls. Green voxels: TBSS skeleton. Red and Yellow voxel: voxels with cannabis users FA > healthy FA (multiple comparison correction, $p = 0.05$). Statistical significance is higher where the color assigned to the voxel is brighter.



Conclusions and future directions

This MRI project focuses on the neurobiological underpinnings of addiction, connecting structural, microstructural and neuropsychological data, showing structural and microstructural abnormalities in young drug users with new insight for the planning of preventive and therapeutic strategies.

National Early Warning System for drugs - N.E.W.S.



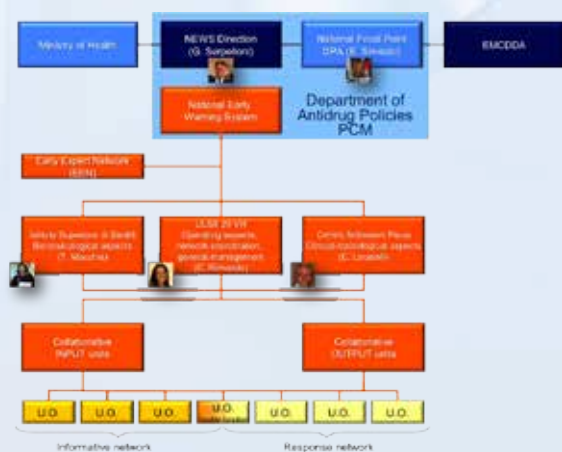
Serpelloni G.¹, Simeoni E.², Macchia T.³, Locatelli C.⁴, Rimondo C.⁵, Seri C.⁵, Cavallini M.⁵, Valvo G.⁵

¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri; ²Punto Focale Italiano - Reitox, Dipartimento Politiche Antidroga, PCM; ³Dipartimento del Farmaco, Istituto Superiore di Sanità, Roma; ⁴Centro Antiveleni di Pavia, IRCCS - Fondazione Salvatore Maugeri, Pavia; ⁵Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga, PCM

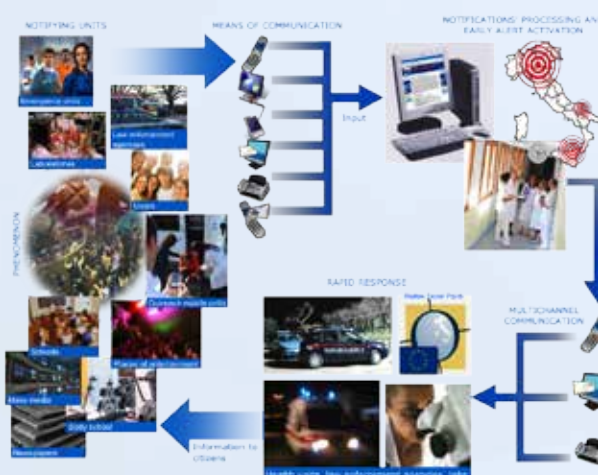
Origin and purpose

With the establishment of the Department for Antidrug Policies of the Italian Presidency of the Council of Ministers, as indicated to the V National Conference on Drugs in Trieste, and in accordance with European directives, the National Early Warning System (N.E.W.S. www.allertadroga.it) in the end of 2008 was activated. The System aimed at early detection of phenomena potentially dangerous to public health, associated with the appearance of new drugs and new pattern of consumption, and to make Alert notifications which promptly involve the departments devoted to the protection and promotion of public health and which are responsible for any implementation of emergency response measures.

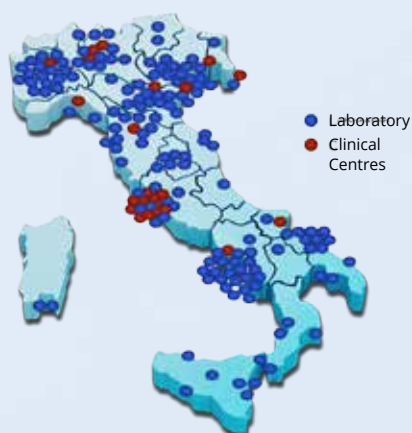
Organizational structure of the National Early Warning System



Macrofunctioning of the Italian National Early Warning System



Geolocation of the Collaborating Centers



Web site allerta.dronet.org



Update of NPS legal status

Following notifications received, as part of the operating procedure for the implementation of health safety measures relating to new psychoactive substances identified by the National Early Warning System, agreed between the Department for Antidrug Policies and the Ministers of Health, from 2010 different decrees were issued to update the Tables of DPR 309/90.

Monitoring of New Psychoactive Substances (NPS)

Since 2009 more than 350 molecules have been intercepted by the National Early Warning System, related to notifications received by the European Monitoring Centre for Drugs and Drug Addiction of Lisbon and the new collaborating centers of the Italian System:

- 101 synthetic cannabinoids
- 6 ketamine and analogues
- 44 synthetic cathinones
- 6 azepane-like
- 75 phenethylamines
- 4 fentanyl analogues
- 11 tryptamines
- 9 synthetic opioids
- 5 piperazines
- 3 phencyclidine analogues

The identification of the New Psychoactive Substances (NPS) is associated with activation of health alert that are sent to the Ministry of Health. The Ministry provides to update the Tables of DPR 309/90 and to issue ordinances. Finally, the Carabinieri section for health protection is activated to monitor compliance of new regulations and the eventual execution of seizures and/or arrests of smugglers and drug dealers.

Clinical cases

The spread of NPS and in particular of synthetic cannabinoids, synthetic cathinones and methoxetamine (an analogue of the anesthetic ketamine) on the Italian area, occurs through commercialization in shops called "smart shops" or through the online sale, and it is highlighted by the notifications to the Early Warning System of acute intoxications related to the consumption of these new drugs.

- Synthetic cannabinoids

From 2010 to today, registered 43 intoxication cases with admission to emergency room (14-66 years; 31 males, 6 females, 6 unknown) related to herbal mixture containing synthetic cannabinoids consumption (smoke).

- Synthetic cathinones

From 2010, registered 8 intoxication cases with admission to emergency room (18-38 years, males) related to synthetic cathinones consumption.

- Methoxetamine

From 2010, registered 17 intoxication cases with admission to emergency room (16-38 years, 11 males) related to methoxetamine consumption.



Ministerial decrees that have made illegal many New Psychoactive Substances from 2010

N	Common name	Ministerial decree
1	JWH-018	
2	JWH-073	
3	Mephedrone	DM 16 June 2010 (G.U. n.146 of 25/6/2010)
4	3,4-Methylenedioxypropylvalerone (MDPV)	
5	JWH-250	
6	JWH-122	DM 11 May 2011 (G.U. n. 112 of 16/5/2011)
7	Structural analogues of 3-phenylacetylindole	
8	Structural analogues of 3-(1-naphthyl)indole	
9	Butylone o bk-MBDB	
10	Structural analogues of 2-amino-1-phenyl-1-propanone	
11	AM-694	DM 29 December 2011 (G.U. n. 3 of 4/1/2012)
12	Structural analogues of 3-benzoylindole	
13	6-monoacetylmorphine o 6-MAM	
14	3-monoacetylmorphine o 3-MAM	
15	Structural analogues of 2-amino-1-phenyl-1-propanone, with one or more substitutions in the aromatic ring, and / or on the nitrogen and / or on the terminal carbon**	DM 11 June 2012 (G.U. n. 142 of 20/6/2012)
16	Methoxyethamine	
17	4-Methylamphetamine	
18	CP 47,497	
19	CP 47,497-omologo C8	DM 24 October 2012 (G.U. n. 264 of 12/11/2012)
20	4-Fluoroamphetamine	
21	5,6-Methylenedioxy-2-aminoindane	
22	5-IT	DM 10 December 2012 (G.U. n. 303 of 31/12/2012)
23	6-APB	
24	5-APB	
25	6-APDB	DM 25 June 2013 (G.U. n. 158 of 8/7/2013)
26	5-APDR	

* With the exclusion of Bupropion and Pyrovalerone

** Replacement of chemical name of the derivative of Butylone

NET-OUTCOME

Treatment monitoring and outcome evaluation



UNODC
United Nations Office on Drugs and Crime

NIDA NATIONAL INSTITUTE
ON DRUG ABUSE



European Monitoring Centre
for Drugs and Drug Addiction



Giovanni Serpelloni, M.D.¹; Maurizio Gomma, M.D.²; Bruno Genetti, M.A.³; Monica Zermiani, M.A.S.⁴; Claudia Rimondo, M.A.S.⁵; Roberto Mollica, M.D.⁶; Jan Gryczynski, Ph.D.⁷; Kevin E. O'Grady, Ph.D.⁸; Robert P. Schwartz, M.D.⁹
¹Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri, Rome, Italy; ²Centro di coordinamento nazionale progetto OUTCOME, Verona, Italy; ³Explora - Centro di Ricerca e Analisi Statistica, Padua; ⁴Dipartimento delle Dipendenze, Azienda ULSS 20 Verona, Italy; ⁵Sistema Nazionale di Allerta Precoce, Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri, Rome, Italy; ⁶Osservatorio Nazionale, Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri, Rome, Italy; ⁷Friends Research Institute, Inc., 1040 Park Avenue, Suite 103 Baltimore, MD 21201, USA; ⁸University of Maryland, College Park, Department of Psychology, College Park, MD 20742, USA

Aim

- Create a network of operating units for the development, monitoring and evaluation of outcome in patients addicted to heroin, related to benefits received from addiction services.
- Promote an evaluation of treatment outcomes.
- Evaluate the effectiveness of different pharmacological treatments currently available to patients addicted to heroin, related to the implemented services (integrated therapies).

Indicators of outcome

- Abstinence from drug use.
- Condition well-being.
- Quality of life.
- Social functioning (work, home, lawlessness and social relations).
- Reduction/absence of risk of death due to overdose or other drug-related causes.
- Reduction/absence of risk behaviors for infectious diseases.

Categories of outcome

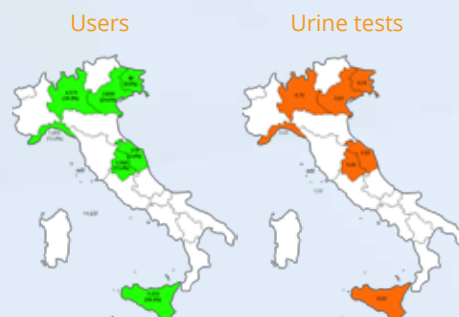
- No Responder: up to 30% drug-free days of treatment.
- Low Responder: from 30% to 60% drug-free days of treatment.
- Responder: beyond 60% drug-free days of treatment.

The Network



Characteristics of patients

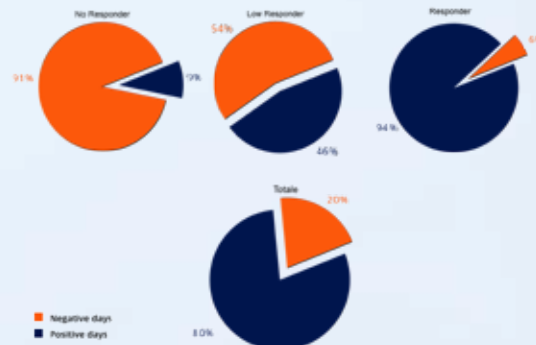
- Males 83,6%; females 16,4%
- Italians 97,5 %
- Africans are the most numerous group among foreigners (0,8%)
- Low grounding level (73,6%)
- Long-term job (63,2 %)
- Live with parents (45,9%), 30,3% with partner and children



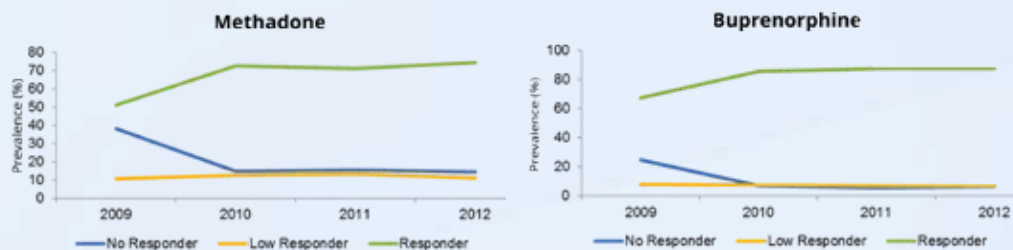
Subjects according to type of treatment, gender and outcome

	No Responder		Low Responder		Responder		Total	
	N. sogg.	%	N. sogg.	%	N. sogg.	%	N. sogg.	%
Methadone								
Male	1.040	83,1	779	80,6	5.337	82,3	7.156	82,2
Female	212	16,9	187	19,4	1.150	17,7	1.549	17,8
Total (%)	1.252	14,4	966	11,1	6.487	74,5	8.705	100,0
Buprenorphine								
Male	154	84,2	164	88,6	2.250	88,1	2.568	87,9
Female	29	15,8	21	11,4	304	11,9	354	12,1
Total (%)	183	6,3	185	6,3	2.554	87,4	2.922	100,0
Total								
Male	1.194	83,2	943	81,9	7.587	83,9	9.724	83,6
Female	241	16,8	208	18,1	1.454	16,1	1.903	16,4
Total (%)	1.435	12,3	1.151	9,9	9.041	77,8	11.627	100,0

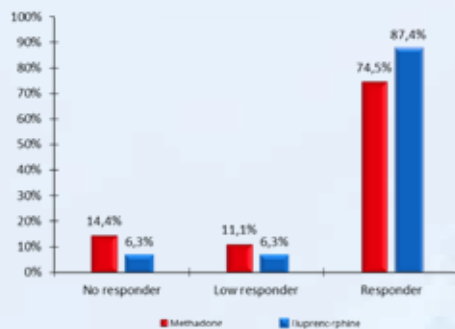
Percentage of drug-free days



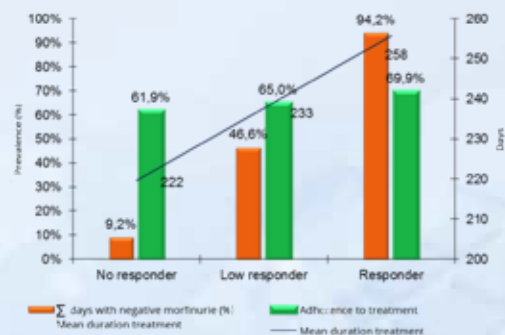
Trend - Percentage of subjects according to type of pharmacological treatment and response (2009, 2010, 2011 e 2012)



Outcome for pharmacological treatment



Mean duration of treatment, outcome and percentage adherence to treatment



Publication



Conclusions

- Substitution therapy with methadone represents the most frequently used treatment.
- Both treatments (methadone and buprenorphine) produce significant results reducing the drug use.
- The greater effectiveness of buprenorphine is related to type of users, assuming it.
- Regularity of urine tests influences positively on abstinence from drug use.

Transcranial Magnetic Stimulation rTMS over the left dorsolateral prefrontal cortex in a group of patients in treatment for alcohol addiction

In collaborazione con



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Background

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive brain stimulation technique that could be effective in addiction treatment. To date, several human studies assessed the effects of rTMS protocols on substances craving and intake, in nicotine, alcohol and cocaine addicts (Bellamoli et al., 2013).

The underlying rationale is that exciting the dorsolateral prefrontal cortex (DLPFC) by high frequency pulses, would increase its activity and its cognitive control function. In particular, with drug-addicted subjects, this treatment would increase the ability to cope with craving (strong desire for drug, that is a major component determining relapse). Moreover, because rTMS can increase the release of dopamine in the mesolimbic dopaminergic system (Strafella et al., 2009), it is assumed that repeated applications of rTMS may affect neuroadaptation induced by the chronic use of substances.

Aim

This research project, promoted by the Italian Department for Antidrug Policies - Presidency of the Council of Ministers and entrusted to the Verona Addiction Department - ULSS 20, aimed to assess the effectiveness of introducing rTMS sessions in a program of hospitalization for the treatment of alcohol addiction, in reducing alcohol consumption and the severity of craving, compared to sham rTMS treatment. As the mechanisms underlying the rTMS are still unclear, psychological and neurophysiological variables were also measured for a more comprehensive assessment of the treatment effects.



Materials and methods

This is a prospective, randomized, single-blind, sham-controlled study.

Participants

Subjects recruited for the study were patients of the 3 weeks hospitalization program occurring at the Unit of Addiction Medicine and Alcoholism Service of the Addiction Department ULSS 20 Verona. Patients were screened in the first week of hospitalization.

20 patients in treatment principally for alcoholism concluded the rTMS sessions: active rTMS was administered to 10 patients and 10 patients received sham stimulation.

Descriptive scores for the socio-demographic characteristics and clinical variables of the real rTMS group and the sham group.

Socio-demographic and clinical variables	Real	Sham
Age - mean (SD)	46.7 (7.7)	43.0 (9.6)
Gender		
Men	8	7
Women	2	3
Handedness		
Right-handed	10	8
Ambidexter	0	2
Years of education - mean (SD)	8.7 (2.5)	11.6 (2.9)
SPM score (A, B, C, D; Caffarra et al., 2003) - mean (SD)	35.9 (7.4)	34.4 (7.4)
Motor threshold - mean (SD)	60.8 (8.3)	58.9 (6.7)

rTMS procedure description

rTMS were delivered using the Magstim Rapid2 device with a focal figure-of-eight coil. Participants were administered 4 sessions (2 each week) of high frequency (10 Hz) rTMS at 100% of Motor Threshold over the left DLPFC. Each session consists of 20 trains of 50 pulses, with inter-train interval of 20s.

The sham group was administered rTMS over the left DLPFC with the same parameters, but using a shielded coil that prevented the passage of the magnetic flux to the scalp.



Assessment

Alcohol intake was assessed through patients' self-reports and controlled through toxicological tests. A Visual Analogue Scale (VAS) was administered in different times in order to measure the severity of subjective alcohol craving. Moreover, we assessed the impact of rTMS on mood and on psychopathological symptoms in addicted patients by means of the Symptom Check List-90-R (SCL-90-R). Participants were administered also two computerized neuropsychological measures of response inhibition (Numeric Stroop task and Go/No-go task). Resting EEG was registered in order to search neurophysiological correlates of the rTMS treatment.

Statistical analysis

Data were analyzed using SPSS version 22.0. Because many data were not normally distributed and because of the low sample size evaluated, we used non-parametric tests (Friedman test, Wilcoxon test, Mann-Whitney U test) to detect differences between the real and sham group, and across different times for each group.

1° week of hospitalization							2° week of hospitalization							3° week of hospitalization					End hospitalization	Follow up
MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI		1 month after
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19		
GROUP A																				
Recruitment & Assessment							real rTMS			real rTMS				real rTMS			real rTMS			Assessment
						t0					t1							t2	t3	
GROUP B																				
Recruitment & Assessment							sham			sham				sham			sham		Assessment	
						t0					t1							t2	t3	

Results

We did not find significant effect ($p > 0.05$) on alcohol subjective craving and consumption. While, we observed a significant reduction ($p < 0.05$) in depressive symptoms only in the real group between the baseline and 1 month follow-up. Furthermore, in the real group there was a significant improvement ($p < 0.05$) of the performance in the Stroop test incongruent condition, immediately after the last session of rTMS, and in the same time we observed a significant increase ($p < 0.05$) in the EEG theta band power.

Numerical Stroop task accuracy of the real group before rTMS (T0), at the end of the treatment (T2) and 1 month later (T3), showed as median and 25th to 75th percentiles.



Discussion

We did not find significant effect on main outcomes (subjective craving and consumption). However, in line with the neuropsychological hypothesis that rTMS can improve inhibitory control, we found a significant improvement in the Stroop task performance in the real group immediately after the end of the rTMS treatment. There is a marked tendency to synchronization in theta band after the real stimulation in comparison with pre-rTMS condition, in accordance with the improvement in cognitive control.

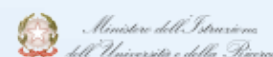
This study has many limitations, first of all the low sample size evaluated. All patients received psycho-social and pharmacological treatment that may interfere with the assessment of craving and intake. Furthermore, apart alcohol, some patients had other addictions, and this also could influence results.

In the future, it may be appropriate to increase the number of sessions of rTMS to be applied to patients.

Analyses of results suggested that further studies are needed to identify the optimal parameters of stimulation for the most effective treatment of drug addiction, to improve our comprehension of the rTMS effects, and to conduct controlled efficacy studies with adequate sample.

Informative Materials for Schools

In collaborazione con



Brain, mind and drugs.
Structure, function, and drug-related alterations

February 2014

Authors: Serpelloni G., Alessandrini F., Zoccatelli G., Rimondo C., Gomma M., Bellamoli E., Cuoghi G.

Brochure aimed to provide information about the normal functioning of the human nervous system and how the use of psychoactive substances is able to alter it, with the intent to explain those mechanisms to readers in a clear and simple way and to encourage a healthy life style, free from drugs and alcohol and from any addiction.



Drug and prevention.
Educational slides for educators and teachers.

This set of slides is an extensive collection of the principal and reasoned scientific evidence available to date on the topic of the dangers and damages resulting from the use of drugs. The material is made available to educators in order to constantly update their knowledge on the topic and be able to use it for information and prevention activities targeted especially parents, teachers and students. A very wide and comprehensive collection of products, allowing you to choose and select the slides useful for the intervention expected, on the basis of the target audience, the topic and the available time.



Postcards Substances

Features: Color 4/4
Size: 10x15 cm
Target: 14-21 years



Folding Multilingual leaflets on substances with exhibitor

Features: Color 4/4
Size: open size 42x29, 7 cm
Available in several languages: Albanian, English, French, Romanian, Serbian-Croatian, Spanish.
Target: 14-21 years



Brochures on substances

Features: Color 4/4
Size: closed size 21x29, 7 cm
Target: senior



Brochure on substances
Datasheets

Features: Printing 4/0
Size: 21x29, 7 cm
Target: 14-21 years



Posters

Available formats:
• 21 x 29.7 cm
• 29 x 42 cm
• 140 x 200 cm

Posters and leaflets
"It's never too early"

Campaign for the early detection
of substance use in young people
for early intervention



Postcard "The drug does not teach"

Features: Color 4/4
Size: 15x10 cm
Target: 6-21 years



Commercials, documentaries and
informational videos

Target: > 14 years

Institutional websites

	Contacts	Visits	Visited pages
Total	108.774.189	80.763.443	6.641.095



dronet.org

Informative website developed by the Department of Antidrug Policies – Presidency of the Council of Ministers that aims at contributing to the public understanding of science by means of a national network on addiction. The website, dedicated to healthcare professionals, teachers, parents and youngsters, intends to examine in depth themes related to drug abuse and addiction through the consultation of evidence-based informative material.

Contacts: 34.777.112

Visited pages: 1.770.356

Visits: 14.972.542

Reference period: January 2009 - March 2014



cocaina.dronet.org

Thematic website aimed at analyzing topics related to both cocaine use and addiction. The website illustrates the effects on the organism deriving from the use of cocaine, correlated pathologies, available therapeutic treatments, epidemiological data on cocaine consumption in both Italy and Europe. One section is dedicated to the in-depth analysis of the legal aspects, norms, and penalties provided in the Highway code in case of drugged driving.

Contacts: 8.957.296

Visited pages: 582.902

Visits: 8.040.597

Reference period: October 2009 - March 2014



alcol.dronet.org

This website intends to analyze different aspects related to both alcohol abuse and addiction which represent serious public health problems and one of the main causes of preventable death. The website elucidates the effects of alcohol on the organism and related pathologies, available treatments, epidemiological data on alcohol consumption in both Italy and Europe and vulnerable risk groups (e.g. youngsters and women).

Contacts: 12.424.635

Visited pages: 871.366

Visits: 11.170.181

Reference period: October 2009 - March 2014



drugfreedu.org

Informative website dedicated to: teachers who are willing to include in their educational-institutional programs some research-based preventative measures in order to respond to students' needs; to parents who can increase their awareness of the drug problem and consult practical manuals containing useful suggestions on how to properly monitor their children and safeguard their health; to youths who can find scientific information on psychoactive substances and on the effects of drug of abuse on the brain.

Contacts: 4.221.378

Visited pages: 411.306

Visits: 3.627.173

Reference period: June 2009 - March 2014



cistacontroledroghe.dronet.org

Initiative developed for raising young people's awareness against drug and alcohol abuse, mafia organizations, their violent actions and terrorism. The website offers an educational spur to young students for a world without drugs and mafias, where intelligence, feelings, emotions and creativity do not need psychoactive or alcoholic substances to be expressed at best.

Contacts: 283.163

Visited pages: 22.874

Visits: 260.644

Reference period: September 2013 - March 2014



neuroscienzedipendenze.it

This informative website was conceived in the framework of the strategies that the Department of Antidrug Policies promotes to increase both the knowledge and awareness of the effects deriving from the use of psychoactive substances, by way of multimedia tools easing the circulation of scientifically reliable news and disclosure of clear, coherent and reliable messages.

Contacts: 4.230.383

Visited pages: 391.182

Visits: 3.850.801

Reference period: October 2009 - March 2014



allerta.dronet.org

The N.E.W.S. website is based on georeference systems of input notifications that are connected to other advanced management systems of output warning notifications. This system allows the detection of both new drugs and new consumption patterns, support the work of emergency departments in case of acute intoxication caused by unknown substances and ease the analytical activity of laboratories.

Contacts: 256.052

Visited pages: 37.546

Visits: 187.967

Reference period: June 2009 - March 2014



drugsonstreet.it

The "Drugs on Street" protocol and the NNIDAC project (National Network on accidents related to Drugs and Alcohol), aims at the prevention of drunk and drugged driving. The main beneficiaries are healthcare professionals and law enforcement officials involved in the project and all the subjects that are interested in the protocol implementation. On the website, it is possible to find legal references to norms regulating and sanctioning drunk and drugged driving, a collection of news concerning the road safety topic and various preventative materials.

Contacts: 1.909.750

Visited pages: 209.689

Visits: 1.676.745

Reference period: October 2009 - March 2014



cannabis.dronet.org

Thematic website aimed at analyzing from a toxicological, neuropsychic, medical and social perspective, the increasingly frequent scientific evidence proving cannabis to be one of the main substances responsible for: the alteration of learning abilities in young people, the decrease of motivation to face life problems, the easy approach to other drugs, the damage of fetus' normal neurologic development in substance abusing mothers and of several other health damages in humans.

Contacts: 8.991.789

Visited pages: 600.717

Visits: 8.310.474

Reference period: June 2011 - March 2014



drogaprevenzione.dronet.org

This website contains all the preventative materials developed so far by the Department of Antidrug Policies, in cooperation with several Italian collaborating centers. This collection has been created to give further options or ideas to all those professionals working in the field of anti-drug prevention and communication, giving the possibility to personalize the materials. On the website, it is possible to find the products regarding information campaigns, dedicated websites, monographs, slide shows and videos/spots.

Contacts: 2.463.258

Visited pages: 161.808

Visits: 2.291.793

Reference period: January 2012 - March 2014



consorzioetico.dronet.org

Website dedicated to drug and alcohol abuse prevention by means of the participation to a national network of Italian municipalities with the goal of promoting health among young people and adults. The "Consorzio Etico" is a bunch of people, administrations, associations from the civil society and from Public Administrations that express in a clear and unequivocal manner their "NO" to the use of all kind of drugs and to alcohol abuse.

Contacts: 329.588

Visited pages: 44.857

Visits: 299.589

Reference period: May 2013 - March 2014



droganograzie.it

This website is addressed to users aged between 11 and 19 years. Every page is distinguished by teenage fiction characters who give their contribution to illustrate and describe the website contents. The website makes a description of the main psychotropic and psychoactive substances by dealing extensively with the "Drugs and brain" topic. On the website it is possible to find a wide collection of both informative and educational materials, oriented to the development of personal skills that can be useful to resist peer pressure.

Contacts: 19.451.642

Visited pages: 957.256

Visits: 16.649.562

Reference period: June 2009 - March 2014



gambling.dronet.org

This website aims at dealing with the pathological gambling problem on the basis of scientific evidence in order to face it by means of a thorough technical-scientific analysis and a multidisciplinary approach that allow to highlight neurobiological, psychobehavioral, social and economical aspects constituting the basis of this phenomenon which is a relevant social problem besides being a public health problem.

Contacts: 1.537.805

Visited pages: 111.605

Visits: 1.443.346

Reference period: May 2013 - March 2014



drogainbreve.dronet.org

Website designed by the National Institute on Drug Abuse, translated and adapted by the Italian Department of Antidrug Policies. It manages simple and concise information on drugs, their effects, prevention strategies and treatments. The website stems from the need to reach a wide audience of users including those with lower education in the light of certain studies who detect in this type of population, together with other problems, a preponderance of alcohol and drug abuse.

Contacts: 2.593.697

Visited pages: 9.198

Visits: 2.338.088

Reference period: August 2012 - March 2014



diagnosiprecoce.dronet.org

This website is addressed to professionals belonging to the operating units which joined the "Early detection" project and to all those who are interested in analyzing the theme of early identification and intervention of substance abuse in minors. On this website it is possible to find informative and educational materials which can be used to face the theme of youth drug use both in the family and in the health environment.

Contacts: 397.337

Visited pages: 44.389

Visits: 364.876

Reference period: October 2012 - March 2014



dreamonshow.it

This website promotes artistic-creative activities in various expressive fields by way of the direct involvement of young people who become active protagonist of the activities themselves. In particular, the dancing sector is characterized by a multi-level project, through which every year more than 500 young dancers are involved. The website is rich in audio, video and photographic materials describing the activities that have been carried out since 2004 to present.

Contacts: 5.949.304

Visited pages: 414.044

Visits: 5.229.065

Reference period: June 2009 - March 2014

Progetto NSP Alert 2013



REGIONE VENETO
ULSS 20
VERONA

Direttore Giuseppina Bonavina



Regione del Veneto - Azienda ULSS 20
Dipartimento delle Dipendenze

Considering the more and more urgent need to tackle the New Psychoactive Substances phenomenon, it is necessary to enhance the activities of the National Early Warning System that have to be directed on the one hand to increasingly improve the notification gathering also in the light of the extension of the network of collaborating centers registered in the last year, on the other hand to make more effective the interventions adopted to cope with the emergence of new substances both in terms of analytical and diagnostic identification.

The NPS ALERT 2013 project aims at extending the areas of activity of the ALERT 2011 project, together with and as an integration of what has already been encompassed in the aforementioned project and in line with the developments that this phenomenon requires by virtue of the size and characteristics that it has acquired over the years.

NPS ALERT 2013, therefore, by keeping active the activities that were already envisaged in the ALERT 2011 project aims at widening and strengthening further areas of activity, independently from ALERT 2011, by analyzing the aspects that, after 2 years of activity, have been identified as crucial to understand the phenomenon of the emergence of new drugs and to activate at a territorial level, the countermeasures in order to prevent and/or decrease all the connected risks and to improve the laboratory abilities of the collaborating operative units.

To this purpose, NPS ALERT 2013 will mainly consider all the activities that concern the management of notification activities and of the network of collaborating centers, of epidemiologic issues (demand/supply on internet and the spreading of consumptions in both the general and student population), the training and the improvement of the diagnostic skills of those who work in laboratories, emergency departments, drug addiction departments, law enforcement units.

Moreover, NPS ALERT 2013 is aimed at examining in depth the web monitoring, in particular of those drugs supply channels (e.g. dark net and illegal rave parties) that escape the controls carried out by Law Enforcement. In so doing, the project creates the opportunity to identify, through the improvement of the knowledge on the topic, new procedures for the activation of control and counter actions carried out by the competent authorities.



THE
ITALIAN SCIENTIFIC
COMMUNITY
ON ADDICTION

Registration to the Community

Italian Scientific Community on Addiction (ISCA) – Professional network for sharing good practices and tool for the promotion of scientific collaborations

To join in, it is necessary to link on www.dpascientificcommunity.it, www.politicheantidroga.it, www.droganews.it e www.dronet.org and fill in the online form. Please, upload your curriculum vitae together with the form. In case an institution or an organization wants to join in, it is necessary to send a brief description of the activities carried out, an updated organization chart, the name of the contact persons. The registration in ISCA entails sharing its principles and objectives and accepting its functions and rules.





PRESIDENZA DEL CONSIGLIO DEI MINISTRI

Dipartimento Politiche Antidroga



SISTEMA NAZIONALE DI ALLERTA PRECOCE

NATIONAL EARLY WARNING SYSTEM - N.E.W.S.

NSP project Alert 2013

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