

**Edoardo Spina**

**CURRICULUM VITAE**

## **DATI PERSONALI**

Luogo di nascita: Castellammare di Stabia (NA)

Data di nascita: 21 febbraio 1956

Residenza: Via Nuova Panoramica dello Stretto 1020, Complesso “Il Parnaso”, 98168 Messina

Stato civile: coniugato, due figli.

## **TITOLI ACCADEMICI**

1981: Laurea in Medicina e Chirurgia presso l'Università di Messina.

1981: Abilitazione all'esercizio della professione di Medico-Chirurgo presso l'Università di Messina.

1985: Specializzazione in Neurologia presso l'Università di Messina.

1987: PhD (Dottorato di ricerca) in Farmacologia Clinica presso il Karolinska Institute di Stoccolma.

1991: Specializzazione in Psichiatria presso l'Università di Messina.

1998: Professore Associato di Farmacologia presso la Facoltà di Medicina e Chirurgia dell'Università di Messina.

2004: Idoneo al ruolo di Professore Universitario di I fascia per il Settore Scientifico- Disciplinare BIO/14 – Farmacologia

2005: Professore Straordinario di Farmacologia presso la Facoltà di Medicina e Chirurgia dell'Università di Messina.

2008: Professore Ordinario di Farmacologia presso la Facoltà di Medicina e Chirurgia dell'Università di Messina.

## **CURRICULUM PROFESSIONALE**

Marzo 1983-Gennaio 1987: borsista e quindi ricercatore presso il Dipartimento di Farmacologia Clinica dell'Ospedale Universitario di Huddinge, Istituto Karolinska, Stoccolma, Svezia.

Gennaio-Marzo 1987: professore visitante di psicofarmacologia presso il Dipartimento di Farmacologia e Psichiatria dell'Università di Extremadura, Badajoz, Spagna.

Aprile 1987-Ottobre 1998: Assistente e, da Aprile 1995, Aiuto di Psichiatria presso i Servizi di Salute Mentale dell'Azienda USL 5 di Messina (ex USL 41).

Giugno 1987-Ottobre 1998: Collaboratore volontario presso l'Istituto di Farmacologia dell'Università di Messina.

Novembre 1998-Maggio 2005: Professore Associato di Farmacologia, Settore Scientifico-Disciplinare BIO/14 ex E07X, presso l'Istituto di Farmacologia della Facoltà di Medicina e Chirurgia dell'Università di Messina e, dal 2001, presso la Sezione di Farmacologia del Dipartimento Clinico Sperimentale di Medicina e Farmacologia dell'Università di Messina.

Giugno 2005: Professore Straordinario di Farmacologia, Settore Scientifico-Disciplinare BIO/14, presso la Sezione di Farmacologia del Dipartimento Clinico Sperimentale di Medicina e Farmacologia dell'Università di Messina.

### **Posizione ed incarichi attuali**

- Professore Ordinario di Farmacologia presso il Dipartimento di Medicina Clinica e Sperimentale dell'Università di Messina.
- Coordinatore del Corso di Laurea in Medicina e Chirurgia dell'Università di Messina (da ottobre 2018).
- Responsabile f.f. (da ottobre 2016 a ottobre 2020) e Responsabile (da novembre 2020) dell'Unità Operativa Semplice Dipartimentale di Farmacologia Clinica dell'Azienda Ospedaliera Policlinico Universitario di Messina.
- Responsabile del Centro Referente per la Segnalazione Spontanea Organizzata della Regione Sicilia (da ottobre 2016)
- Responsabile scientifico del Centro Regionale di Farmacovigilanza, Regione Sicilia (da ottobre 2016)
- Responsabile aziendale di farmacovigilanza, Azienda Ospedaliera Policlinico Universitario di Messina (da ottobre 2016)

## **ATTIVITA' SCIENTIFICA**

Svolge attività di ricerca nel settore della neuropsicofarmacologia clinica, con particolare riferimento al metabolismo ed alla farmacocinetica degli psicofarmaci. E' autore di 254 pubblicazioni su riviste scientifiche indicizzate, di 3 libri, di 28 capitoli di libro e di oltre 400 abstracts relativi a partecipazioni a congressi nazionali ed internazionali.

H index: **60**

Numero totale di citazioni: **10721** (31 maggio 2022)

Le principali linee di ricerca sono:

- Farmacocinetica degli antidepressivi, degli antipsicotici e degli antiepilettici
- Interazioni farmacocinetiche degli psicofarmaci
- Farmacogenetica e personalizzazione della terapia in psichiatria
- Monitoraggio terapeutico degli psicofarmaci
- Farmacovigilanza, farmacoutilizzazione e farmacoepidemiologia in psichiatria
- Studi clinici sull'efficacia e sulla tollerabilità degli psicofarmaci in pazienti con patologie psichiatriche

### **Direzione strutture di ricerca**

- Dal 2005 al 2010 responsabile scientifico (insieme ai Proff. A.P. Caputi e S. Cuzzocrea) della Linea di ricerca Neurofarmacologia-Neuroepidemiologia-Farmacovigilanza dell'IRCCS Istituto Neurolesi "Bonino-Pulejo" di Messina.
- Dal 2013 ad oggi coordinatore del Gruppo di Lavoro di Neuropsicofarmacologia della Società Italiana di Farmacologia (insieme ai Proff. M. Riva, R. Molteni).

### **Finanziamenti**

#### *Pubblici*

- Borsa di studio della Fondazione "Bonino-Pulejo" nel 1982.
- EU Biomed 1 (contratto BMH1-CT94-1622) per il triennio 1995-1997. Titolo: Early identification factors responsible for the interindividual variability in drug metabolism in man. Coordinatore: Prof. G.M. Pacifici, Università di Pisa.

- EU Biomed 2 (contratto BMH4-CT96-0291) per il triennio 1996-1998. Titolo: Metabolism and clinical effects of psychotropic drugs: from molecular genetics to patient care. Coordinatore: Prof. L. Bertilsson, Istituto Karolinska, Stoccolma.
- Istituto Superiore di Sanità, 1996-1998: Progetto “Proprietà fisico-chimiche dei medicinali e loro sicurezza d’uso” Coordinatore: Prof. E. Perucca, Università di Pavia.
- PRA 1999: Progetto “Valutazione dell’utilità della fenotipizzazione e della genotipizzazione per il citocromo P450 2D6 nella risposta ai farmaci antipsicotici”.
- PRIN 2000: Progetto “Genotipizzazione per il CYP2C9 in pazienti trattati con l’anticoagulante orale warfarina” nell’ambito del progetto “Parametri farmacogenetici, farmacocinetici e farmacodinamici determinati l’effetto anticoagulante della warfarina nell’uomo”. Coordinatore: Prof. R. Padrini, Università di Padova
- PRA 2000: Progetto “Interazioni farmacocinetiche tra nuovi antidepressivi ed antipsicotici in vitro ed in vivo”.
- PRA 2001: Progetto “Impatto di fattori genetici, fisiologici e della concomitante somministrazione di altri psicofarmaci sulla cinetica degli enantiomeri di fluoxetina e norfluoxetina”
- PRA 2002: Progetto “Ruolo del polimorfismo genetico dell’isoenzima 2D6 del citocromo P450 nella risposta clinica agli inibitori delle colinesterasi in pazienti con Malattia di Alzheimer”.
- PRA 2003: Progetto “Valutazione dell’effetto inducente dell’oxcarbazepina sul metabolismo dei nuovi farmaci antipsicotici”.
- PRIN 2004: Progetto “Biologia molecolare della glucuronidazione della morfina nell’eroinomane” nell’ambito del progetto “Ruolo dei glucuronidi della morfina nella dipendenza da eroina”. Coordinatore: Prof. A. Badiani, Università di Roma.
- PRA 2004: Progetto “Correlazione tra concentrazioni plasmatiche e risposta clinica in pazienti schizofrenici trattati con olanzapina”.
- PRA 2005: “Interazioni farmacocinetiche tra quetiapina e stabilizzatori dell’umore”.
- PRA 2006-07: Progetto “Effetto di un trattamento con antipsicotici atipici sui livelli serici di Brain-Derived Neurotrophic Factor (BDNF) in pazienti schizofrenici”.
- PRIN 2007: Progetto “Tipizzazione genetica degli isoenzimi del citocromo P450 e monitoraggio plasmatico degli antidepressivi in pazienti depressi in oncologia” nell’ambito del progetto “Caratterizzazione fenotipica dell’adattamento mentale al cancro e della risposta al trattamento con farmaci antidepressivi in oncologia” Coordinatore: Prof. Tullio Giraldi, Università di Trieste.
- PRA 2008-2009: Effetto di melatonina ed iperico su comportamento e neurogenesi in un modello animale di depressione

- AIFA Ricerca Indipendente sui Farmaci 2012: Studio controllato randomizzato sulle implicazioni farmacocinetiche e cliniche della sostituzione di prodotti generici di farmaci antiepilettici. Coordinatore: Prof. Emilio Perucca, Università di Pavia.
- Progetto Regionale di Farmacovigilanza, finanziato fondi AIFA 2010-2011: Valutazione del profilo di tollerabilità e sicurezza dei farmaci antipsicotici in età pediatrica.
- Ministero della Salute, Progetto ricerca finalizzata: Towards precision medicine in psychiatry: clinical validation of a combinatorial pharmacogenomics approach (RF-2016-02361697). Coordinatore: Prof. Massimo Gennarelli, Università di Brescia.
- Progetto Multiregionale di Farmacovigilanza, finanziato fondi AIFA 2012-2014 (responsabile scientifico per la regione Sicilia): Valutazione post-marketing del profilo beneficio-rischio dei farmaci biologici Originator e biosimilari in area dermatologica, reumatologica, gastroenterologica ed oncoematologica tramite la costruzione di un network unico multiregionale per l'analisi integrata di dati provenienti da banche dati sanitarie, sorveglianze attive e registri clinici – progetto VALORE
- Progetto Multiregionale di Farmacovigilanza finanziato, fondi AIFA 2012-2014 (responsabile scientifico per la regione Sicilia): Integrazione Ospedale – territorio nelle popolazioni a rischio: riconciliazione terapeutica e counselling farmacologico (MEAP 3.0)

#### *Privati*

- 2007 Lundbeck S.p.A. Interazioni farmacocinetiche tra antidepressivi e nuovi antipsicotici.
- 2009 Boehringer Ingelheim Italia S.p.A. Psicofarmaci e neuro plasticità.
- 2009 Lundbeck S.p.A. Interazioni farmacocinetiche tra antidepressivi e farmaci internistici.
- 2011 Innova Pharma S.p.A. Modelli sperimentali preclinici applicati allo studio della neuroplasticità da psicofarmaci.
- 2013 Lundbeck S.p.A. Antipsicotici di seconda generazione: concentrazioni plasmatiche di steady-state in pazienti trattati con farmaci generici e di marca.
- 2014 ArcaPharma s.r.l. Integratori alimentari nel trattamento dei disturbi depressivi.
- 2015 ArcaPharma s.r.l. Integratori alimentari nel trattamento dei disturbi psichici.
- 2016 ArcaPharma s.r.l. Integratori alimentari nel trattamento dei disturbi psichici.

#### **Attività editoriale e recensione di manoscritti**

Dal 2020 Editor-in-Chief di CNS & Neurological Disorders-Drug Targets (CNSND-DT)

Dal 2010 Associate Editor di Frontiers in Pharmacogenetics.

Dal 2000 è nell'Editorial Board della rivista Therapeutic Drug Monitoring.

Dal 2006 è nell'Editorial Board di Basic and Clinical Pharmacology and Toxicology.

Dal 2007 al 2009 nell'Editorial Board di Pharmacological Research.

Dal 2016 nell'Editorial Board di CNS & Neurological Disorders-Drug Targets (CNSND-DT)

Dal 2010 nell'Editorial Board di Clinical Neuropsychopharmacology and Therapeutics

Dal 2015 nell'Editorial Board di Neuropsychiatric Disease and Treatment

Dal 2016 nell'Editorial Board di CNS & Neurological Disorders-Drug Targets (CNSND-DT)

Dal 2016 nel Board of International Consulting Editors di Journal of Clinical Psychopharmacology

Dal 2017 nell'Editorial Board di European Journal of Clinical Pharmacology

Dal 2022 nell'Editorial Board di di International Clinical Psychopharmacology

Svolge inoltre attività di referee per le numerose riviste di neuropsichiatria fra cui:

Acta Neuropsychiatrica, Acta Pharmacologica Sinica, Analytica Chimica Acta, British Journal of Clinical Pharmacology, Clinical Drug Investigation, Clinical Pharmacokinetics, Clinical Pharmacology and Therapeutics, CNS Drugs, Drugs of Today, Drug Safety, Epilepsia, European Psychiatry, Expert Opinion for Drug Delivery, Expert Opinion on Pharmacotherapy, Expert Review of Neurotherapeutics, General Hospital Psychiatry, International Journal of Neuropsychopharmacology, Journal of Chromatography B, Journal of Clinical Psychiatry, Journal of Pharmacokinetics and Pharmacodynamics, Journal of Psychiatry & Neuroscience, Journal of Psychiatry Research, Journal of Psychopharmacology, Life Sciences, Neuropsychopharmacology, Pharmacogenetics, Pharmacogenetics and Genomics , Pharmacogenomics, Pharmacopsychiatry, Progress in Neuro-Psychopharmacology & Biological Psychiatry, Psychopharmacology, Psychotherapy and Psychosomatics

### **Incarichi in società scientifiche**

- Componente del Direttivo e Segretario della Sezione di Farmacologia Clinica della Società Italiana di Farmacologia (dal 2003 al 2007).
- Componente del Direttivo della European Association for Clinical Pharmacology and Therapeutics (dal 2011 al 2017).

## **ATTIVITA' DIDATTICA**

1987: Corso di Psicofarmacologia nel Dipartimento di Farmacologia e Psichiatria dell'Università di Estremadura, Badajoz, Spagna.

1990-91, 1991-92: Corso di Farmacologia Clinica, scuola per infermieri professionali, U.S.L. 41 Messina.

1991-92, 1992-93, 1993-94: Professore a contratto di Farmacologia Speciale e Farmacocinetica presso la Scuola di Specializzazione in Farmacologia dell'Università di Messina.

1994-95, 1995-96: Professore a contratto di Neuropsicofarmacologia presso la Scuola di Specializzazione in Farmacologia della Seconda Università di Napoli.

Dal 1998 insegnamento della farmacologia presso l'Università di Messina:

### *Corsi di Laurea della Facoltà di Medicina e Chirurgia*

- Corso di Laurea in Medicina e Chirurgia (in atto Coordinatore del C.I. di Farmacologia, Tossicologia e Medicina Basata sulle Evidenze)
- Corso di Laurea in Tecniche di Neurofisiopatologia
- Corso di Laurea in Scienze delle Professioni Sanitarie Tecniche e Diagnostiche
- Corso di Laurea in Tecniche Audioprotesiche

### *Scuole di Specializzazione*

- Direttore della Scuola di Specializzazione in Farmacologia dell'Università degli Studi di Messina dal 2004 al 2007
- Coordinatore della Scuola di Specializzazione in Farmacologia Medica dell'Università degli Studi di Catania (sede amministrativa), per la sede aggregata dell'Università degli Studi di Messina, dal 2008 al 2018.

Docente presso le seguenti Scuole di Specializzazione:

- Farmacologia e Tossicologia Clinica
- Psichiatria
- Neurologia
- Neurofisiopatologia
- Medicina Fisica e Riabilitazione
- Neuropsichiatria Infantile
- Genetica Medica
- Geriatria
- Anestesia e Rianimazione
- Biochimica Clinica
- Radioterapia

### *Dottorato di Ricerca*



- Componente del Collegio dei Docenti del Dottorato di Ricerca in Medicina Sperimentale dell'Università di Messina dal 1999 al 2001
- Componente del Collegio dei Docenti del Dottorato di Ricerca in Farmacologia Clinica dell'Università di Perugia consorziata con l'Università di Messina dal 2001 al 2008
- Coordinatore del Dottorato di Ricerca in Psicofarmacologia Clinica dell'Età Evolutiva dell'Università di Messina dal 2009 (XXIV e XXV ciclo)
- Coordinatore del Dottorato di Ricerca in Neuropsicofarmacologia Clinica e Sperimentale ed Applicazioni in Neuroriabilitazione dell'Università di Messina dal 2011 (XXVI, XXVII e XXVIII ciclo)
- Coordinatore del Dottorato di Ricerca in Scienze Biomediche Cliniche e Sperimentali dell'Università di Messina dal 2014 al 2018 (XXIX, XXX, XXXI, XXXII e XXXIII ciclo)
- Componente del PhD program in Translational Molecular Medicine and Surgery (dal 2019)

E' stato inoltre docente presso vari Corsi di Perfezionamento e Master.

Svolge inoltre attività tutoriale ed ha seguito numerosi allievi nello svolgimento di tesi sperimentali sia per il Corso di Laurea in Medicina e Chirurgia che in diverse Scuole di Specializzazione.

#### *Corsi ECM*

Dal 2000 ad oggi ha partecipato come docente ad oltre 200 corsi ECM relativi a tematiche di neuro psicofarmacologia clinica. Di 25 corsi ECM è stato anche organizzatore e responsabile scientifico.

## **ATTIVITA' ASSISTENZIALE**

- Componente dell'Unità Operativa di Farmacologia Clinica, Farmacoepidemiologia e Farmacovigilanza dell'Azienda Ospedaliera Policlinico Universitario di Messina (dal 1998 al 2003).
- Responsabile dell'Unità Operativa Semplice di Tossicologia e Monitoraggio Farmaci e Sostanze d'Abuso dell'Azienda Ospedaliera Policlinico Universitario di Messina da Luglio 2003 a Giugno 2009.
- Componente e vice-direttore dell'Unità Operativa di Farmacologia Clinica dell'Azienda Ospedaliera Policlinico Universitario di Messina (dal 2010 al 2016).
- Componente del Centro Interdipartimentale d'Informazione Farmaco-Tossicologico dell'Università di Messina (dal 1999 al 2003).

## **ATTIVITA' ISTITUZIONALE**

- Componente del Nucleo di Valutazione dell'Università di Messina (dal 2005 al 2007).
- Preside vicario della Facoltà di Medicina e Chirurgia dell'Università di Messina (dal 2009 al 2012).
- Componente, con ruolo di vice presidente e segretario scientifico, del Comitato Etico dell'Azienda Ospedaliera Policlinico Universitario di Messina dal 2006 al 2013.
- Presidente del Comitato Etico interaziendale della Provincia di Messina da gennaio 2014 a giugno 2020.

## ELENCO DELLE PUBBLICAZIONI

### PUBBLICAZIONI SU RIVISTE SCIENTIFICHE INDICIZZATE

1. Pisani F, **Spina E**, Trunfio C, Fazio A, Oteri G, Di Perri R. Intradaily oscillations in dipropylacetic acid plasma levels with two or three daily doses of dipropylacetamide in epileptic patients. *Ital J Neurol Sci* 1983; 2: 173-177.
2. **Spina E**, Goransson M. Effect of antiepileptic drugs on the 2-hydroxylation of desmethylimipramine in human liver microsomes. *IRCS Med Sci* 1984; 12: 1123-1124.
3. **Spina E**, Birgersson C, von Bahr C, Ericsson O, Mellstrom B, Steiner E, Sjoqvist F. Phenotypic consistency in hydroxylation of desmethylimipramine and debrisoquine in healthy subjects and in human liver microsomes. *Clin Pharmacol Ther* 1984; 36: 677-682.
4. **Spina E**, Henthorn TK, Eleborg L, Nordin C, Sawe J. Desmethylimipramine overdose: nonlinear kinetics in a slow hydroxylator. *Ther Drug Monit* 1985; 7: 239-241.
5. **Spina E**, Ericsson O, Nordin C, Analysis of tricyclic antidepressants in serum and plasma yields similar results. *Ther Drug Monit* 1985; 7: 242-243.
6. von Bahr C, **Spina E**, Birgersson C, Ericsson O, Henthorn T, Goransson M, Sjoqvist F. Inhibition of desmethylimipramine 2-hydroxylation by drugs in human liver microsomes. *Biochem Pharmacol* 1985; 34: 2501-2505.
7. **Spina E**, Koike Y. Differential effects of cimetidine and ranitidine on imipramine demethylation and desmethylimipramine hydroxylation by human liver microsomes. *Eur J Clin Pharmacol* 1986; 30: 239-242.
8. **Spina E**, Pacifici GM, von Bahr C, Rane A. Characterization of desmethylimipramine 2-hydroxylation in human foetal and adult liver microsomes. *Acta Pharmacol et Toxicol* 1986; 58: 277-281.
9. von Bahr C, Birgersson C, Morgan ET, Ericsson O, Goransson M, **Spina E**, Woodhouse K. Oxidation of tricyclic antidepressant drugs, debrisoquine and 7-ethoxyresorufin, by human liver preparations. *Xenobiotica* 1986; 16: 391-400.
10. Pisani F, Primerano G, Amendola D'Agostino A, **Spina E**, Fazio A. Valproic acid-amitriptyline interaction in man. *Ther Drug Monit* 1986; 8: 382-383.
11. Pisani F, Fazio A, **Spina E**, Artesi C, Pisani B, Russo M, Trio R, Perucca E. Pharmacokinetics of the antidepressant drug viloxazine in normal subjects and in epileptic patients receiving chronic anticonvulsant treatment. *Psychopharmacology* 1986; 90: 295-298.
12. **Spina E**, Steiner E, Ericsson O, Sjoqvist F. Hydroxylation of desmethylimipramine: dependence on the debrisoquine hydroxylation phenotype. *Clin Pharmacol Ther* 1987; 41: 314-319.
13. Fazio A, **Spina E**, Pisani F. Analysis of tricyclic antidepressants by liquid chromatography. *J Liq Chromatogr* 1987; 10: 223-240.
14. Tomson T, **Spina E**, Wedlund JE. Minor additive inducing effects of phenobarbital on carbamazepine clearance in patients on combined carbamazepine-phenytoin therapy. *Ther Drug Monit* 1987; 9: 117-1197.
15. **Spina E**, Arena A, Pisani F. Urinary desipramine hydroxylation index and steady-state plasma concentrations of imipramine and desipramine. *Ther Drug Monit* 1987; 9: 129-133.
16. Steiner E, **Spina E**. Differences in the inhibitory effect of cimetidine on desipramine metabolism between rapid and slow debrisoquine hydroxylators. *Clin Pharmacol Ther* 1987; 42: 278-282.
17. **Spina E**, Kenneback G, Bergfeldt L, Tomson T. Prevalence of cardiac conduction disturbances during carbamazepine treatment: preliminary data. *Functional Neurology* 1987; 2: 563-567.
18. Bertilsson L, Aberg-Wistedt A, Otani K, **Spina E**. Alprazolam does not inhibit the metabolism of nortriptyline in depressed patients. *Ther Drug Monit* 1988; 10: 231-233.

19. Fazio A, Artesi C, Lorefice C, Oteri G, Romano F, Russo M, **Spina E**, Trio R, Pisani F. Evaluation of tricyclic antidepressants plasma levels by an automated enzyme immunoassay in comparison with a high performance liquid chromatographic method. *Ther Drug Monit* 1988; 10: 333-339.
20. Steiner E, Dumont E, **Spina E**, Dahlqvist R. Inhibition of desipramine 2-hydroxylation by quinidine and quinine. *Clin Pharmacol Ther* 1988; 43: 577-581.
21. **Spina E**, Tomson T, Bertilsson L, Svensson JO, Faigle JW. Single-dose kinetics of an enteric coated formulation of carbamazepine-10,11-epoxide. *Ther Drug Monit* 1988; 10: 382-385.
22. Pisani F, Fazio A, Oteri G, **Spina E**, Perucca E, Bertilsson L. Effect of valpromide on the pharmacokinetics of carbamazepine-10,11-epoxide. *Br J Clin Pharmacol* 1988; 25: 611-613.
23. **Spina E**, Buemi AL, Caputi AP, Benitez J, Cobaleda J, Garcia MA, Llerena A, Pinas B. Debrisoquine oxidation in schizophrenic patients treated with neuroleptics. *Pharmacological Research Communications* 1988; 20: 1103-1104.
24. Perucca E, Pisani F, **Spina E**, Oteri G, Fazio A, Bertilsson L. Effects of valpromide and viloxazine on the elimination of carbamazepine-10,11-epoxide, an active metabolite of carbamazepine. *Pharmacological Research* 1989; 21: 111-112.
25. Henthorn TK, **Spina E**, Dumont E, von Bahr C. In vitro inhibition of a polymorphic human liver P-450 isozyme by narcotic analgesic. *Anesthesiology* 1989; 70: 339-342.
26. **Spina E**, Buemi AL, Sanz E, Bertilsson L. Diazepam treatment does not influence the debrisoquine or mephenytoin phenotyping tests. *Ther Drug Monit* 1989; 11: 721-723.
27. Schepis C, Palazzo R, Ragusa RM, **Spina E**, Barletta C. Association of cutis verticis gyrata with fragile X syndrome and fragility of chromosome 12. *Lancet* 1989; I: 279.
28. **Spina E**. Pharmacogenetics of tricyclic antidepressants. *Rev Farmacol Clin Exp* 1989; 6: 143-146.
29. Pisani F, Caputo M, Fazio A, Oteri G, Russo M, **Spina E**, Perucca E, Bertilsson L. Interaction of carbamazepine-10,11-epoxide, an active metabolite of carbamazepine, with valproic acid: a pharmacokinetic study. *Epilepsia* 1990; 31: 339-342.
30. Schepis C, Palazzo R, Cannavò SP, Ragusa RM, Barletta C, **Spina E**. Prevalence of primary cutis verticis gyrata in a psychiatric population: association with chromosomal fragile sites. *Acta Derm Venereol* 1990; 70: 483-486.
31. **Spina E**, Amendola D'Agostino AM, Ioculano MP, Oteri G, Fazio A, Pisani F. No effect of thioridazine on plasma concentrations of carbamazepine and its active metabolite carbamazepine-10,11-epoxide. *Ther Drug Monit* 1990; 12: 511-513.
32. **Spina E**, Martines C, Fazio A, Trio R, Pisani F, Tomson T. Effect of phenobarbital on the pharmacokinetics of carbamazepine-10,11-epoxide, an active metabolite of carbamazepine. *Ther Drug Monit* 1991; 13: 109-112.
33. **Spina E**, Martines C, Caputi AP, Cobaleda J, Pinas B, Carrillo A, Benitez J. Debrisoquine oxidation phenotype during neuroleptic monotherapy. *Eur J Clin Pharmacol* 1991; 41: 467-470.
34. **Spina E**, Sturiale V, Ancione M, Valvo S, Masessa De Dovitiis G, Di Rosa AE, Meduri M, Caputi AP. Haloperidol-induced acute dystonic reactions in hospitalised psychiatric patients: incidence and risk factors. *New Trends Exp Clin Psychiat* 1991; 7: 101-106.
35. **Spina E**, Campo GM, Calandra S, Caputi AP, Carrillo A, Benitez J. Debrisoquine oxidation in an Italian population: a study in healthy subjects and in schizophrenic patients. *Pharmacol Res* 1992; 25: 43-50.
36. **Spina E**, Ancione M, Di Rosa AE, Meduri M, Caputi AP. Polymorphic debrisoquine oxidation and acute neuroleptic-induced side effects. *Eur J Clin Pharmacol* 1992; 42: 347-348.
37. **Spina E**, Campo GM, Avenoso A, Pollicino AM, Caputi AP. Interaction between fluvoxamine and imipramine/desipramine in four patients. *Ther Drug Monit* 1992; 14: 194-196.

38. **Spina E**, Campo GM, Avenoso A, Pollicino AM, Caputi AP. Effect of buspirone or zopiclone on plasma concentration of imipramine and desipramine in depressed patients. *Eur Bull Drug Res* 1992; 1: 37-40.
39. Pollicino AM, **Spina E**, Campo GM, Avenoso A, Caputi AP. Pharmacokinetic interaction between tricyclic antidepressants and other psychotropic drugs in depressed patients. *Pharmacol Res* 1992; 25 (Suppl 2): 210-211.
40. **Spina E**, Avenoso A, Pollicino AM, Fazio A, Pisani F, Caputi AP. No effect of fluvoxamine or fluoxetine on plasma concentrations of carbamazepine in epileptic patients. *Pharmacol Res* 1992; 25 (Suppl 2): 214-215.
41. **Spina E**, De Domenico P, Bonanzinga M, Amendola D'Agostino MA, Gitto C, Di Rosa AE, Caputi AP. A double blind comparative study of bromperidol versus haloperidol in schizophrenic patients. *New Trends Exp Clin Psychiat* 1992; 8: 67-71.
42. Pisani F, Fazio A, Artesi C, Oteri G, **Spina E**, Tomson T, Perucca E. Impairment of carbamazepine-10,11-epoxide elimination by valnoctamide, a valpromide isomer, in healthy subjects. *Br J Clin Pharmacol* 1992; 34: 85-87.
43. Kenneback G, Bergfeldt L, Tomson T, **Spina E**, Edhag O. Carbamazepine induced bradycardia - a problem in general or only in susceptible patients? A 24-h long-term electrocardiogram study. *Epilepsy Res* 1992; 13: 141-145.
44. Garofalo G, Ragusa RM, Barletta C, **Spina E**. Schizophrenia and chromosomal fragile sites. *Am J Psychiatry* 1992; 8: 1116.
45. **Spina E**, Sturiale V, Valvo S, Ancione M, Di Rosa AE, Meduri M, Caputi AP. Debrisoquine oxidation phenotype and neuroleptic-induced dystonic reactions. *Acta Psychiatr Scand* 1992; 86: 364-366.
46. **Spina E**, Sturiale V, Valvo S, Ancione M, Di Rosa AE, Meduri M, Caputi AP. Prevalence of acute dystonic reactions associated with neuroleptic treatment with and without anticholinergic prophylaxis. *Int Clin Psychopharmacol* 1993; 8: 21-24.
47. **Spina E**, Pollicino AM, Avenoso A, Campo GM, Caputi AP, Perucca E. Effect of fluvoxamine on the pharmacokinetics of imipramine and desipramine in healthy subjects. *Ther Drug Monit* 1993; 15: 243-246.
48. **Spina E**, Avenoso A, Pollicino AM, Caputi AP, Fazio A, Pisani F. Coadministration of carbamazepine with fluoxetine or fluvoxamine. *Ther Drug Monit* 1993; 15: 247-250.
49. Furlanut M, Benetello P, **Spina E**. Pharmacokinetic optimisation of antidepressant therapy. *Clin Pharmacokinet* 1993; 24: 301-318.
50. **Spina E**, Pollicino AM, Avenoso A, Campo GM, Caputi AP. Fluvoxamine-induced alterations in plasma concentrations of imipramine and desipramine in depressed patients. *Int J Clin Pharm Res* 1993; 13: 167-171.
51. Palazzo R, Schepis C, Ruggeri M, Baldini L, Pizzimenti A, Arcoraci V, **Spina E**. An endocrinological study in patients with primary cutis verticis gyrata. *Acta Derm Venereol* 1993; 73: 348-349.
52. Garofalo G, Ragusa RM, Argiolas A, Scavuzzo C, **Spina E**, Barletta C. Evidence of chromosomal fragile sites in schizophrenic patients. *Ann Genet* 1993; 36: 132-135.
53. **Spina E**, Ancione M, Di Rosa AE, Artemisia A, Natoli C, Caputi AP. Iron status in schizophrenic patients with acute neuroleptic-induced dystonic reactions. *Progr Neuro-Psychopharmacol Biol Psychiat* 1994; 18: 891-898.
54. **Spina E**, Caputi AP. Pharmacogenetic aspects in the metabolism of psychotropic drugs: pharmacokinetic and clinical implications. *Pharmacol Res* 1994; 29: 121-137.
55. **Spina E**, Campo GM, Avenoso A, Caputi AP, Zuccaro GM, Gatti G, Strada G, Bartoli A, Perucca E. CYP2D6-related oxidation polymorphism in Italy. *Pharmacol Res* 1994; 29: 281-289.

56. **Spina E**, Avenoso A, Campo GM, Caputi AP, Perucca E. Decreased plasma concentrations of imipramine and desipramine following cholestyramine intake in depressed patients. *Ther Drug Monit* 1994; 16: 432-434.
57. Perucca E, Gatti G, **Spina E**. Clinical pharmacokinetics of fluvoxamine. *Clin Pharmacokinet* 1994; 27: 175-190.
58. **Spina E**, Perucca E. Newer and older antidepressants. A comparative review of drug interactions. *CNS Drugs* 1994; 2: 479-497.
59. **Spina E**, De Domenico P, Ruello C, Longobardo N, Ancione M, Gitto C, Di Rosa AE, Caputi AP. Adjunctive fluoxetine in the treatment of negative symptoms in chronic schizophrenic patients. *Int Clin Psychopharmacol* 1994; 9: 281-285.
60. Pisani F, Xiao B, Fazio A, **Spina E**, Perucca E, Tomson T. Single dose pharmacokinetics of carbamazepine-10,11-epoxide in patients on lamotrigine monotherapy. *Epilepsy Research* 1994; 19: 245-248.
61. Perucca E, Gatti G, Cipolla G, **Spina E**, Barel S, Soback S, Gips M, Bialer M. Inhibition of diazepam metabolism by fluvoxamine: a pharmacokinetic study in normal volunteers. *Clin Pharmacol Ther* 1994; 56: 471-476.
62. **Spina E**, Avenoso A, Campo GM, Caputi AP, Perucca E. The effect of carbamazepine on the 2-hydroxylation of desipramine. *Psychopharmacology* 1995; 17: 413-416.
63. Di Rosa AE, Morgante L, **Spina E**, Meduri M. Epidemiology and pathoetiology of neurological syndromes with hyperthermia. *Functional Neurology* 1995; 10: 111-119.
64. De Domenico P, Di Rosa AE, **Spina E**, Amendola D'Agostino A, Bonanzinga M, Ruello C, Clementi A, Serra S, Meduri M. Genetics of schizophrenia: an update. *New Trends Exp Clin Psychiat* 1995; 11: 135-150.
65. **Spina E**, Avenoso A, Campo GM, Caputi AP, Perucca E. Phenobarbital induces the 2-hydroxylation of desipramine. *Ther Drug Monit* 1996; 18: 60-64.
66. **Spina E**, Pisani F, Perucca E. Clinically significant drug interactions with carbamazepine: an update. *Clin Pharmacokinet* 1996; 31: 198-214.
67. **Spina E**, Gitto C, Avenoso A, Campo GM, Caputi AP, Perucca E. Relationship between plasma desipramine levels, CYP2D6 phenotype and clinical response to desipramine: a prospective study. *Eur J Clin Pharmacol* 1997; 51: 395-398.
68. **Spina E**, Avenoso A, Campo GM, Scordo MG, Caputi AP, Perucca E. Effect of ketoconazole on the pharmacokinetics of imipramine and desipramine in healthy subjects. *Br J Clin Pharmacol* 1997; 43: 315-318.
69. Avenoso A, **Spina E**, Campo G, Facciola G, Ferlito M, Zuccaro P, Perucca E, Caputi AP. Interaction between fluoxetine and haloperidol: pharmacokinetic and clinical implications. *Pharmacol Res* 1997; 35: 335-339.
70. **Spina E**, Arena D, Scordo G, Fazio A, Pisani F, Perucca E. Elevation of plasma carbamazepine concentrations by ketoconazole in epileptic patients. *Ther Drug Monit* 1997; 19: 535-538.
71. Zuccaro P, Pacifici R, Altieri I, Avenoso A, Pellegrini M, **Spina E**, Perucca E, Pichini S. Issues in methodology and applications for therapeutic drug monitoring of fluoxetine and norfluoxetine enantiomers in treated patients. *Ther Drug Monit* 1998; 20: 20-24.
72. **Spina E**, Avenoso A, Facciola G, Fabrazzo M, Monteleone P, Maj M, Perucca E, Caputi AP. Effect of fluoxetine on the plasma concentrations of clozapine and its major metabolites in patients with schizophrenia. *Int Clin Psychopharmacol* 1998; 13: 141-145.
73. Avenoso A, Facciola G, Campo GM, Fazio A, **Spina E**. Determination of clozapine, N-desmethylclozapine, and clozapine N-oxide in human plasma by reverse phase high-performance liquid chromatography with ultraviolet detection. *J Chromatogr B Biomed Appl* 1998; 714: 299-308.

74. Avenoso A, Facciola G, Scordo MG, Gitto C, Drago Ferrante G, Madia AG, **Spina E**. No effect of citalopram on plasma concentrations of clozapine, risperidone and their active metabolites in patients with chronic schizophrenia. *Clin Drug Invest* 1998; 16: 393-398.
75. Facciola G, Avenoso A, **Spina E**, Perucca E. Inducing effect of phenobarbital on clozapine metabolism in patients with chronic schizophrenia. *Ther Drug Monit* 1998; 20: 628-630.
76. De Domenico P, Di Rosa AE, Amendola D'Agostino A, Martino G, Meduri M, **Spina E**. The effect of clozapine on aggressive behaviour in patients with chronic schizophrenia. *Int J Psych Clin Pract* 1999; 3: 49-54.
77. Facciola G, Avenoso A, Scordo MG, Madia AG, Ventimiglia A, Perucca E, **Spina E**. Small effects of valproic acid on the plasma concentrations of clozapine and its major metabolites in patients with schizophrenic or affective disorders. *Ther Drug Monit* 1999; 21: 341-345.
78. Avenoso A, Facciola G, Scordo MG, **Spina E**. No effect of the new antidepressant reboxetine on CYP2D6 activity in healthy volunteers. *Ther Drug Monit* 1999; 21: 577-579.
79. Scordo MG, **Spina E**, Facciola G, Avenoso A, Johansson I, Dahl ML. CYP2D6 genotype and steady-state plasma levels of risperidone and 9-hydroxyrisperidone. *Psychopharmacology* 1999; 147: 300-305.
80. Pisani F, **Spina E**, Oteri G. Antidepressant drugs and seizure susceptibility: from in vitro data to clinical practice. *Epilepsia* 1999; 40 Suppl 10: 48-56.
81. **Spina E**, Avenoso A, Facciola G, Scordo MG, Ancione M, Madia AG, Ventimiglia A, Perucca E. Relationship between plasma concentrations of clozapine and norclozapine and therapeutic response in patients with schizophrenia resistant to conventional neuroleptics. *Psychopharmacology* 2000; 148: 83-89.
82. **Spina E**, Avenoso A, Facciola G, Salemi M, Scordo MG, Giacobello T, Madia AG, Perucca E. Plasma concentrations of risperidone and 9-hydroxyrisperidone: effect of comedication with carbamazepine or valproate. *Ther Drug Monit* 2000; 22: 481-485.
83. Avenoso A, Facciola G, Salemi M, **Spina E**. Determination of risperidone and its major metabolite 9-hydroxy-risperidone in human plasma by reversed phase liquid chromatography with ultraviolet detection. *J Chromatogr B Biomed Appl* 2000; 746: 173-181.
84. **Spina E**, Avenoso A, Salemi M, Facciola G, Scordo MG, Ancione M, Madia AG. Plasma concentrations of clozapine and its major metabolites during combined treatment with paroxetine or sertraline. *Pharmacopsychiatry* 2000; 33: 213-217.
85. Scordo GM, **Spina E**, Romeo P, Dahl ML, Bertilsson L, Johansson I, Sjoqvist F. CYP2D6 genotype and antipsychotic-induced extrapyramidal side-effects in schizophrenic patients. *Eur J Clin Pharmacol* 2000; 56: 679-683.
86. **Spina E**, Scordo MG, Avenoso A, Perucca E. Adverse drug interaction between risperidone and carbamazepine in a patient with chronic schizophrenia and deficient CYP2D6 activity. *J Clin Psychopharmacol* 2001; 21: 108-109.
87. **Spina E**, Avenoso A, Facciola G, Salemi M, Scordo MG, Ancione M, Madia AG, Perucca E. Relationship between plasma risperidone and 9-hydroxyrisperidone concentrations and clinical response in patients with schizophrenia. *Psychopharmacology* 2001; 153: 238-243.
88. **Spina E**, Avenoso A, Facciola G, Scordo MG, Ancione M, Madia A. Plasma concentrations of risperidone and 9-hydroxyrisperidone during combined treatment with paroxetine. *Ther Drug Monit* 2001; 23: 223-227.
89. Kirchheiner J, Brosen K, Dahl ML, Gram LF, Kasper S, Roots I, Sjoqvist F, **Spina E**, Brockmoller J. CYP2D6 and CYP2C19 genotype-based dose recommendations for antidepressants: a first step towards subpopulation specific dosages. *Acta Psychiatr Scand* 2001; 104: 173-192.
90. Scordo MG, Aklillu E, Yasar U, Dahl ML, **Spina E**, Ingelman-Sundberg M. Genetic polymorphism of cytochrome P450 2C9 in a Caucasian and Black-African population. *Br J Clin Pharmacol* 2001; 52: 447-450.

91. Yasui-Furukori N, Hidestrand M, **Spina E**, Facciola G, Scordo MG, Tybring G. Different enantioselective 9-hydroxylation of risperidone by two human CYP2D6 and CYP3A4 enzymes. *Drug Metab Dispos* 2001; 29: 1263-1268.
92. Brandolese R, Scordo MG, **Spina E**, Gusella M, Padrini R. Severe phenytoin intoxication in a homozygous CYP2C9\*3 metabolizer. *Clin Pharmacol Ther* 2001; 70: 391-394.
93. **Spina E**, Avenoso A, Scordo MG, Ancione M, Madia A, Levita A. No effect of reboxetine on plasma concentrations of clozapine, risperidone and their active metabolites. *Ther Drug Monit* 2001; 23: 675-678.
94. **Spina E**, Scordo MG. Newer antipsychotics. Comparative review of drug interactions. *Expert Rev Neurotherapeutics* 2001; 1: 171-182.
95. Scordo MG, **Spina E**. Cytochrome P450 polymorphisms and response to antipsychotic therapy. *Pharmacogenomics* 2002; 3: 201-218.
96. **Spina E**, Perucca E. Clinical significance of pharmacokinetic interactions between antiepileptic and psychotropic drugs. *Epilepsia* 2002; 43 suppl 2: 37-44.
97. **Spina E**, Scordo MG. Clinically significant drug interactions with antidepressants in the elderly. *Drugs & Aging* 2002; 19: 299-320.
98. **Spina E**, Avenoso A, Scordo MG, Ancione M, Madia A, Gatti G, Perucca E. Inhibition of risperidone metabolism by fluoxetine in patients with schizophrenia: a clinically relevant pharmacokinetic drug interaction. *J Clin Psychopharmacol* 2002; 22: 419-423.
99. Jannuzzi G, Gatti G, Magni P, **Spina E**, Pacifici R, Zuccaro PG, Torta R, Guarneri L, Perucca E. Plasma concentrations of the enantiomers of fluoxetine and norfluoxetine: sources of variability and preliminary observations on relationships with clinical response. *Ther Drug Monit* 2002; 24: 616-627.
100. Scordo MG, Pengo V, **Spina E**, Dahl ML, Gusella M, Padrini R. Influence of cytochrome P450s 2C9 and 2C19 genetic polymorphisms on warfarin maintenance dose and metabolic clearance. *Clin Pharmacol Ther* 2002; 72: 702-710.
101. Morgante L, Epifanio A, **Spina E**, Di Rosa AE, Zappia M, Basile G, La Spina P, Quattrone A. Quetiapine versus clozapine: a preliminary report of comparative effects on dopaminergic psychosis in patients with Parkinson's disease. *Neurol Sci* 2002; 23: S89-S90.
102. Gatti G, Bonomi I, Marchiselli R, Fattore C, **Spina E**, Scordo G, Pacifici R, Perucca E. An improved stereoselective assay for the determination of fluoxetine and norfluoxetine enantiomers in human plasma by high-performance liquid chromatography. *J Chromatogr B Analyt Technol Biomed Life Sci* 2003; 784: 375-383.
103. D'Amico G, Cedro C, Muscatello MR, Pandolfo L, Di Rosa AE, Zoccali R, La Torre D, D'Arrigo C, **Spina E**. Olanzapine augmentation of paroxetine-refractory Obsessive-compulsive disorder. *Progr Neuro-Psychopharmacol Biol Psychiat* 2003; 27: 619-623.
104. **Spina E**, Scordo MG, D'Arrigo C. Metabolic drug interactions with new psychotropic agents. *Fundam Clin Pharmacol* 2003; 17: 517-538.
105. Zoccali R, Muscatello MR, La Torre D, Malara G, Canale A, Crucitti D, D'Arrigo C, **Spina E**. Lack of pharmacokinetic interaction between mirtazapine and the newer antipsychotics clozapine, risperidone and olanzapine in patients with chronic schizophrenia. *Pharmacol Res* 2003; 48: 411-414.
106. Gagliano A, Germanò E, Pustorino G, Impallomeni C, D'Arrigo C, Calamoneri F, **Spina E**. Risperidone treatment of children with autistic disorder: effectiveness, tolerability and pharmacokinetic implications. *J Child Adolesc Psychopharmacol* 2004; 14: 41-49.
107. Zoccali R, Muscatello MR, Cedro C, Neri P, La Torre D, **Spina E**, Di Rosa AE, Meduri M. The effect of mirtazapine augmentation of clozapine in the treatment of negative symptoms of schizophrenia: a double-blind, placebo-controlled study. *Int Clin Psychopharmacol* 2004; 19: 71-76.



108. **Spina E**, Perugi G. Antiepileptic drugs: indications other than epilepsy. *Epileptic Disord* 2004; 6: 57-75.
109. Scordo MG, Caputi AP, D'Arrigo C, Fava G, **Spina E**. Allele and genotype frequencies of CYP2C9, CYP2C19 and CYP2D6 in an Italian population. *Pharmacol Res* 2004 50: 195-200.
110. Morgante L, Basile G, Epifanio A, **Spina E**, Antonimi A, Stocchi F, Di Rosa E, Martino G, Marconi R, La Spina P, Nicita-Mauro V, Di Rosa AE. Continuous apomorphine infusion (CAI) and neuropsychiatric disorders in patients with advanced Parkinson's disease: a follow-up of two years. *Arch Gerontol Geriatr Suppl* 2004; 9: 291-296.
111. **Spina E**, D'Arrigo C, Migliardi G, Morgante L, Zoccali R, Ancione M, Madia M. Plasma risperidone concentrations during combined treatment with sertraline. *Ther Drug Monit* 2004; 26: 386-390.
112. Morgante L, Epifanio A, **Spina E**, Zappia M, Di Rosa AE, Marconi R, Basile G, Di Raimondo G, La Spina P, Quattrone A. Quetiapine and clozapine in parkinsonian patients with dopaminergic psychosis. *Clin Neuropharmacol* 2004; 27: 153-156.
113. Galatti L, Giustini SE, Sessa A, Polimeni G, Salvo F, **Spina E**, Caputi AP. Neuropsychiatric reactions to drugs: an analysis of spontaneous reports from general practitioners in Italy. *Pharmacol Res* 2005; 51: 211-216.
114. Trifirò G, **Spina E**, Brignoli O, Sessa E, Caputi AP, Mazzaglia G. Antipsychotic prescribing pattern among Italian general practitioners: a population-based study during 1999-2002 years. *Eur J Clin Pharmacol* 2005; 61: 47-53.
115. Muscatello MR, Pacetti M, Cacciola M, La Torre D, Zoccali R, D'Arrigo C, Migliardi G, **Spina E**. Plasma concentrations of risperidone and olanzapine during coadministration with oxcarbazepine. *Epilepsia* 2005; 46: 771-774.
116. Scordo MG, **Spina E**, Dahl ML, Gatti G, Perucca E. Influence of CYP2C9, 2C19 and 2D6 genetic polymorphisms on the steady state plasma concentrations of the enantiomers of fluoxetine and norfluoxetine. *Basic Clin Pharmacol Toxicol* 2005; 97: 296-301.
117. D'Arrigo C, Migliardi G, Santoro V, Morgante L, Muscatello MR, Ancione M, **Spina E**. Effect of fluvoxamine on plasma risperidone concentrations in patients with schizophrenia. *Pharmacol Res* 2005; 52: 497-501.
118. Polimeni G, Salvo F, Cutroneo P, Nati G, Russo A, Giustini SE, **Spina E**. Venlafaxine-induced urinary incontinence resolved after switching to sertraline. *Clin Neuropharmacol* 2005; 28: 247-248.
119. Scordo MG, Dahl ML, **Spina E**, Cordici F, Arena MG. No association between CYP2D6 polymorphism and Alzheimer's disease in an Italian population. *Pharmacol Res* 2006; 53: 162-165.
120. Olie JP, **Spina E**, Murray S, Yang R. Ziprasidone and amisulpride effectively treat negative symptoms of schizophrenia: results of a 12-week, double-blind study. *Int Clin Psychopharmacol* 2006; 21: 143-151.
121. D'Arrigo C, Migliardi G, Santoro V, **Spina E**. Determination of olanzapine in human plasma by reversed-phase high-performance liquid chromatography with ultraviolet detection. *Ther Drug Monit* 2006; 28: 388-393.
122. Galatti L, Polimeni G, Salvo F, Romani M, Sessa A, **Spina E**. Short-term memory loss associated with rosuvastatin. *Pharmacotherapy* 2006; 26: 1190-1192.
123. **Spina E**, D'Arrigo C, Migliardi G, Santoro V, Muscatello MR, Micò U, D'Amico G, Perucca E. Effect of adjunctive lamotrigine treatment on the plasma concentrations of clozapine, risperidone and olanzapine in patients with schizophrenia or bipolar disorder. *Ther Drug Monit* 2006; 28: 599-602.
124. **Spina E**, de Leon J. Metabolic drug interactions with newer antipsychotics: a comparative review. *Basic & Clin Pharmacol & Toxicol* 2007; 100: 4-22.

125. Galatti L, Mazzaglia G, Greco A, Sessa E, Cricelli C, Schito GC, Nicoletti G, **Spina E**, Caputi AP. Co-prescriptions with itraconazole and fluconazole as a signal for possible risk of drug-drug interactions: a four-year analysis from Italian general practice. *Pharmacoepidemiol Drug Saf* 2007; 16: 422-428.
126. Trifirò G, Barbui C, **Spina E**, Moretti S, Tari M, Alacqua M, Caputi AP, Arcoraci V. Antidepressant drugs: prevalence, incidence, indication of use in general practice of Southern Italy during the years 2003-2004. *Pharmacoepidemiol Drug Saf* 2007; 16: 552-559.
127. Migliardi G, D'Arrigo C, Santoro V, Bruno A, Cortese L, Campolo D, Cacciola M, **Spina E**. Effect of topiramate on plasma concentrations of clozapine, olanzapine, risperidone and quetiapine in patients with psychotic disorders. *Clin Neuropharmacol* 2007; 30: 107-113.
128. Guzey C, Scordo MG, **Spina E**, Spigset O. Antipsychotic-induced extrapyramidal symptoms in patients with schizophrenia: associations with dopamine and serotonin receptor and transporter polymorphisms. *Eur J Clin Pharmacol* 2007; 63: 233-241.
129. **Spina E**, Trifirò G. Preventing drug interactions with antidepressants in the elderly. *Aging Health* 2007; 3: 231-243.
130. Zoccali R, Muscatello MR, Bruno A, Cambria R, Micò U, **Spina E**, Meduri M. The effect of lamotrigine augmentation of clozapine in a sample of treatment-resistant schizophrenic patients: a double-blind, placebo-controlled study. *Schizophrenia Res* 2007; 93: 109-116.
131. Polimeni G, Cutroneo P, Gallo A, Gallo S, **Spina E**, Caputi AP. Rabeprazole and psychiatric symptoms. *Ann Pharmacother* 2007; 41:1315-1317.
132. **Spina E**, Cavallaro R. The pharmacology and safety of paliperidone extended-release in the treatment of schizophrenia. *Exp Opin Drug Safety* 2007; 6: 651-662.
133. Savica R, Beghi E, Mazzaglia G, Innocenti F, Brignoli O, Cricelli C, Caputi AP, Musolino R, **Spina E**, Trifirò G. Prescribing patterns of antiepileptic drugs in Italy: a nationwide population-based study in the years 2000-2005. *Eur J Neurol* 2007; 14: 1317-1321.
134. Alacqua M, Trifirò G, Arcoraci V, Germanò E, Magazù A, Calarese T, De Vita G, Gagliano C, **Spina E**. Use and tolerability of newer antipsychotics and antidepressants: a chart review in a psychiatric setting. *Pharm World Sci* 2008; 30: 44-50.
135. Sacchetti E, Trifirò G., Caputi AP, Turrina C, **Spina E**, Cricelli C, Brignoli O, Sessa E, Mazzaglia G. Risk of stroke with typical and atypical antipsychotics: a retrospective cohort study including unexposed subjects. *J Psychopharmacol* 2008; 22: 39-46.
136. Gunes A, Dahl ML, **Spina E**, Scordo MG. Further evidence for the association between 5HT<sub>2C</sub> receptor gene polymorphisms and extrapyramidal side effects in male schizophrenic patients. *Eur J Clin Pharmacol* 2008; 64: 477-482.
137. Diaz FJ, Santoro V, **Spina E**, Cogollo M, Rivera TE, Botts S, de Leon J. Estimating the size of the effects of co-medications on plasma clozapine concentrations using a model that controls for clozapine doses and confounding variables. *Pharmacopsychiatry* 2008; 41: 81-91.
138. Santoro V, D'Arrigo C, Migliardi G, Muscatello MR, Micò U, Cambria R, **Spina E**. Therapeutic drug monitoring of quetiapine: effect of coadministration with antiepileptic drugs in patients with psychiatric disorders. *Open Clin Chem J* 2008; 1: 17-21.
139. **Spina E**, Zoccali R. Sertindole: pharmacological and clinical profile and role in the treatment of schizophrenia. *Expert Opin Drug Metab Toxicol* 2008; 4: 629-638.
140. Trifirò G, Savica R, Morgante L, Tari M, Moretti S, Galdo M, Vanacore N, **Spina E**, Caputi AP, Arcoraci V. Prescribing pattern of Anti-Parkinson drugs in Southern Italy: cross-sectional analysis in the years 2003-2005. *Parkinsonism Relat Disord* 2008; 14: 420-425.
141. Botts S, Diaz FJ, Santoro V, **Spina E**, Muscatello MR, Cogollo M, Castro FE, de Leon J. Estimating the effects of co-medications on plasma olanzapine concentrations by using a mixed model. *Progr Neuro-Psychopharmacol Biol Psychiat* 2008; 32: 1453-1458.
142. **Spina E**, Santoro V, D'Arrigo C. Clinically relevant pharmacokinetic drug interactions with second-generation antidepressants: an update. *Clin Ther* 2008; 30: 1206-1227.

143. Gunes A, **Spina E**, Dahl ML, Scordo MG. *ABCB1* polymorphisms influence steady state plasma levels of 9-hydroxyrisperidone and risperidone active moiety. *Ther Drug Monit* 2008; 30: 628-633.
144. Trifirò G, **Spina E**, Gambassi G. Use of antipsychotics in elderly patients with dementia: do atypical and conventional agents have a similar safety profile? *Pharmacol Res* 2009; 59: 1-12.
145. Alacqua M, Trifirò G, **Spina E**, Moretti S, Tari D, Bramanti P, Caputi AP, Arcoraci V. Newer and older antiepileptic drug use in Southern Italy: a population based study during the years 2003-2005. *Epilepsy Res* 2009; 85: 107-113.
146. de Leon J, **Spina E**, Diaz FJ. Pharmacokinetic drug interaction studies must consider pharmacological heterogeneity, use repeated dosing and be translated into a message understandable to practicing clinicians. *J Clin Psychopharmacol* 2009; 29: 201-205.
147. Migliardi G, **Spina E**, D'Arrigo C, Gagliano A, Germanò E, Siracusano R, Diaz FJ, de Leon J. Short- and long-term effects on prolactin of risperidone and olanzapine treatments in children and adolescents. *Progr Neuro-Psychopharmacol Biol Psychiat* 2009; 33: 1496-1501.
148. **Spina E**, D'Arrigo C, Santoro V, Muscatello MR, Pandolfo G, Zoccali R, Diaz FJ, de Leon J. Effect of valproate on olanzapine plasma concentrations in patients with bipolar or schizoaffective disorder. *Ther Drug Monit* 2009; 31: 758-763.
149. **Spina E**, Fava G, Makos X. Off-label use of second-generation antipsychotics. *Clin Neuropsychiatry* 2009; 6: 11-20.
150. Mondello S, Italiano D, Giacobbe MS, Mondello P, Trimarchi G, Aloisi C, Bramanti P, **Spina E**. Glutamine-supplemented total parenteral nutrition improves immunological status in anorectic patients. *Nutrition* 2010; 26: 677-681.
151. Oteri A, Trifirò G, Gagliostro MS, Tari DU, Moretti S, Bramanti P, **Spina E**, Caputi AP, Arcoraci V. Prescribing pattern of antiepileptic drugs in an Italian setting of elderly outpatients: a population-based study during 2004-2007. *Br J Clin Pharmacol* 2010; 70: 514-522.
152. de Leon J, Diaz F, **Spina E**. Pharmacokinetic drug-drug interactions between olanzapine and valproate needs to be better studied. *J Clin Psychiatry* 2010; 71: 957-958.
153. Crupi R, Mazzon E, Marino A, La Spada G, Bramanti P, Cuzzocrea S, **Spina E**. Melatonin treatment mimics the antidepressant action in chronic-corticosterone treated mice. *J Pineal Res* 2010; 49: 123-129.
154. Migliardi G, **Spina E**, D'Arrigo C, Gagliano A, Germanò E, Siracusano R, Diaz FJ, de Leon J. Reply to Lian et al. *Progr Neuro-Psychopharmacol Biol Psychiat* 2010; 34: 1159.
155. Santoro V, D'Arrigo C, Micò U, Muscatello MR, Zoccali R, **Spina E**. Effect of adjunctive duloxetine on the plasma concentrations of clozapine, olanzapine and risperidone in patients with psychotic disorders. *J Clin Psychopharmacol* 2010; 30: 634-636.
156. Gagliano A, Aricò I, Calarese T, Conurso R, Germanò E, Cedro C, **Spina E**, Silvestri R. Restless leg syndrome in ADHD children: levetiracetam as a reasonable therapeutic option. *Brain Dev* 2011; 33: 480-486.
157. Crupi R, Mazzon E, Marino A, La Spada G, Bramanti P, Battaglia F, Cuzzocrea S, **Spina E**. *Hypericum perforatum* treatment: effect on behaviour and neurogenesis in a chronic stress model in mice. *BMC Compl Altern Med* 2011, 11:7.
158. Muscatello MR, Bruno A, Pandolfo G, Micò U, Scimeca G, Romeo VM, Santoro V, **Spina E**, Zoccali R. Effect of aripiprazole augmentation of clozapine in schizophrenia: a double-blind, placebo-controlled study. *Schizophrenia Res* 2011; 127: 93-99.
159. Crisafulli C, Fabbri C, Porcelli S, Drago A, **Spina E**, De Ronchi D, Serretti A. Pharmacogenetics of antidepressants. *Front Pharmacol* 2011; 2: 1-21.
160. **Spina E**, Crupi R. Safety and efficacy of paliperidone extended-release in acute and maintenance treatment of schizophrenia. *J Centr Nerv Syst Dis* 2011; 3: 27-41.
161. Muscatello MR, Bruno A, Pandolfo G, Micò U, Scimeca G, Di Nardo F, Santoro V, Settineri S, **Spina E**, Zoccali R. Effect of aripiprazole augmentation of serotonin reuptake inhibitors in

- treatment-resistant obsessive-compulsive disorder: a double-blind, placebo-controlled study. *J Clin Psychopharmacol* 2011; 31: 174-179.
162. Caraci F, Crupi R, Drago F, **Spina E**. Metabolic drug interactions between antidepressants and anticancer drugs: focus on selective serotonin reuptake inhibitors and hypericum extract. *Curr Drug Metab* 2011; 12: 570-577.
163. Trifirò G, **Spina E**. Age-related changes in pharmacodynamics: focus on drug acting on central nervous and cardiovascular systems. *Curr Drug Metab* 2011; 12: 611-620.
164. Crupi R, Mazzon E, Marino A, La Spada G, Bramanti P, **Spina E**, Cuzzocrea S. Melatonin's stimulatory effect on adult hippocampal neurogenesis persists after ovariectomy. *J Pineal Res* 2011; 51: 353-360.
165. Porcelli S, Fabbri C, De Ronchi D, **Spina E**, Serretti A. Genetic polymorphisms of cytochrome P450 enzymes and antidepressant metabolism. *Exp Opin Drug Metab Toxicol* 2011; 7: 1101-1115.
166. Micò U, Bruno A, Pandolfo G, Romeo MV, Mallamace D, D'Arrigo C, **Spina E**, Zoccali RA, Muscatello MR. Duloxetine as adjunctive treatment to clozapine in patients with schizophrenia: a randomized, placebo-controlled trial. *Int Clin Psychopharmacol* 2011; 26: 303-310.
167. Crupi R, Cambiaghi M, Deckelbaum R, Hansen I, Mindes J, **Spina E**, Battaglia F. n-3 fatty acids prevents impairment of neurogenesis and synaptic plasticity in BAFF transgenic mice. *Prevent Med* 2012; 54 Suppl: S103-107.
168. **Spina E**, Trifirò G, Caraci F. Clinically significant drug interactions with newer antidepressants. *CNS Drugs* 2012; 26: 39-67.
169. Diaz FJ, Cogollo MR, **Spina E**, Santoro V, Rendon DM, de Leon J. Drug dosage individualization based on a random-effects linear model. *J Biopharm Stat* 2012; 22: 463-484.
170. Richarz U, Jacobs A, **Spina E**. How frequently are contraindicated or warned against combinations of drugs prescribed to patients receiving long-term opioid therapy for chronic pain? *Pharmacoepidemiol Drug Saf* 2012; 21: 453-462.
171. Muscatello MR, **Spina E**, Bandelow B, Baldwin DS. Clinically relevant drug interactions in anxiety disorders. *Hum Psychopharmacol Clin Exp* 2012; 27: 239-253.
172. de Leon J, Santoro V, D'Arrigo C, **Spina E**. Interactions between antiepileptics and second-generation antipsychotics. *Exp Opin Drug Metab Toxicol* 2012; 8: 311-334.
173. Bruno A, Micò U, Pandolfo G, Mallamace D, Abenavoli E, Di Nardo F, D'Arrigo C, **Spina E**, Zoccali R, Muscatello MR. Lamotrigine augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder: a double-blind, placebo-controlled study. *J Psychopharmacol* 2012; 26: 1456-1462.
174. Trifirò G, Tillati S, **Spina E**, Ferrajolo C, Alacqua M, Aguglia E, Caputi AP, Cricelli C, Samani F. A nationwide prospective study on prescribing pattern of antidepressant drugs in Italian primary care. *Eur J Clin Pharmacol* 2013; 69: 227-236.
175. de Leon J, **Spina E**, Diaz FJ. Clobazam therapeutic drug monitoring: a comprehensive review of the literature with proposals to improve future studies. *Ther Drug Monit* 2013; 35: 30-47.
176. Poluzzi E, Raschi E, Koci A, Moretti U, **Spina E**, Behr ER, Sturkenboom M, De Ponti F. Antipsychotic and torsadogenic risk: signals emerging from the FDA adverse event reporting system database *Drug Saf* 2013; 36: 467-479.
177. Calati R, Crisafulli C, Balestri M, Serretti A, **Spina E**, Calabrò M, Sidoti A, Albani D, Massat I, Höfer P, Amital D, Juven-Wetzler A, Kasper S, Zohar J, Souery D, Montgomery S, Mendlewicz J. Evaluation of the role of *MAPK1* and *CREB1* polymorphisms on treatment resistance, response and remission in mood disorder patients. *Progr Neuro-Psychopharmacol Biol Psychiat* 2013; 44: 271-278.
178. Crupi R, Abusamra Y, **Spina E**, Calapai G. Preclinical data supporting/refuting the use of *Hypericum Perforatum* in the treatment of depression. *CNS Neurol Disord Drug Target* 2013; 12: 474-486.

179. Trifirò G, Italiano D, Alibrandi A, Sini G, Ferrajolo C, Capuano A, **Spina E**, Rossi A; The Caserta and L'Aquila groups. Effects of L'Aquila earthquake on the prescribing pattern of antidepressant and antipsychotic drugs. *Int J Clin Pharm* 2013; 35: 1053-1062.
180. Calabrò RS, Bramanti P, **Spina E**, Italiano D. Can zinc depletion play a role in LEV-induced hair loss? Considerations from a case study. *Epilepsy & Behav* 2013; 29: 254-255.
181. Cutroneo PM, Italiano D, Trifirò G, Tortorella G, Russo A, Isola S, Caputi AP, **Spina E**. Acute cerebellar ataxia following meningococcal group C conjugate vaccination. *J Child Neurol* 2014; 29: 128-130.
182. Muscatello MR, Pandolfo G, Micò U, Lamberti Castronuovo E, Abenavoli E, Scimeca G, **Spina E**, Zoccali R, Bruno A. Augmentation of clozapine with ziprasidone in refractory schizophrenia: a double-blind, placebo controlled study. *J Clin Psychopharmacol* 2014; 34: 129-133.
183. Germanò E, Italiano I, Lamberti M, Guerriero L, Privitera C, D'Amico G, Siracusano R, Ingrassia M, **Spina E**, Calabrò MP, Gagliano A. ECG parameters in children and adolescents treated with aripiprazole and risperidone. *Progr Neuro-Psychopharmacol Biol Psychiat* 2014; 51: 23-27.
184. Sultana J, Italiano D, **Spina E**, Cricelli C, Lapi F, Pecchioli S, Gambassi G, Trifirò G. Changes in the prescribing pattern of antidepressant drugs in elderly patients: an Italian, nationwide, population-based study. *Eur J Clin Pharmacol* 2014; 70: 469-478.
185. **Spina E**, de Leon J. Clinically relevant interactions between newer antidepressants and second-generation antipsychotics. *Exp Opin Drug Metab Toxicol* 2014; 10: 721-746.
186. Diaz FJ, Eap CB, Ansermot N, Crettol S, **Spina E**, de Leon J. Can valproic acid be an inducer of clozapine metabolism? *Pharmacopsychiatry* 2014; 47: 89-96.
187. Bruno A, Zoccali R, Abenavoli E, Pandolfo G, Scimeca G, **Spina E**, Muscatello MRA. Augmentation of clozapine with agomelatine in partial-responder schizophrenia: a 16-week, open label, uncontrolled pilot study. *J Clin Psychopharmacol* 2014; 34: 491-494.
188. Italiano I, Ferlazzo E, Gasparini S, **Spina E**, Mondello S, Labate A, Gambardella A, Aguglia U. Generalized versus partial reflex seizures. A review. *Seizure* 2014; 7: 512-520.
189. Trifirò G, Sultana J, **Spina E**. Are the safety profiles of antipsychotic drugs used in dementia the same? An updated review of observational studies. *Drug Saf* 2014; 37: 501-520.
190. Ferlazzo E, Italiano D, Belcastro V, Gasparini S, **Spina E**, Aguglia U. Transient global amnesia as a presenting aura or epilepsy? *Headache* 2014; 7: 1233-1235.
191. Bruno A, Zoccali R, Bellinghieri PM, Pandolfo G, De Fazio P, **Spina E**, Muscatello MR. Reboxetine adjuvant therapy in patients with schizophrenia showing a suboptimal response to clozapine: a 12-week, open-label, pilot study. *J Clin Psychopharmacol* 2014; 34: 620-623.
192. Italiano D, **Spina E**, de Leon J. Pharmacokinetic and pharmacodynamic interactions between antiepileptics and antidepressants. *Exp Opin Drug Metab Toxicol* 2014; 10: 1457-1489.
193. degli Esposti L, Sangiorgi D, Mencacci C, **Spina E**, Pasina C, Alacqua M, la Tour F. Pharmacological utilisation and related costs of drugs used to treat schizophrenia and bipolar disorder in Italy: the IBIS study. *BMC Psychiatry* 2014; 14: 282.
194. **Spina E**, de Leon J. Clinical applications of CYP genotyping in psychiatry. *J Neur Transm* 2015; 122: 5-28.
195. Crisafulli C, Drago A, Calabrò M, **Spina E**, Serretti A. A molecular pathway analysis informs the genetic background at risk for schizophrenia. *Progr Neuro-Psychopharmacol Biol Psychiat* 2015; 59: 21-30.
196. Abusamra Y, Scuruchi M, Habibatni S, Maammeri Z, Benayache S, D'Ascola A, Avenoso A, Campo GM, **Spina E**. Evaluation of putative cytotoxic activity of crude extracts from *Onopordum acanthium* leaves and *Spartium junceum* flowers against the U-373 glioblastoma cell line. *Pak J Pharm Sci* 2015; 28: 1225-1232.

197. Italiano D, Capuano A, Alibrandi A, Ferrara R, Cannata A, Trifirò G, Sultana J, Ferrajolo C, Tari M, Tari DU, Perrotta M, Pagliaro C, Rafaniello C, **Spina E**, Arcoraci V. Indications of newer and older antiepileptic drug use: findings from Southern Italian general practice setting from 2005-2011. *Br J Clin Pharmacol* 2015; 79: 10-19.
198. Serpe L, Canaparo R, Scordo MG, **Spina E**. Pharmacogenetics of drug-metabolizing enzymes in Italian populations. *Drug Metabol Drug Interact* 2015; 30: 107-120.
199. Lamberti M, Italiano D, Guerriero L, D'Amico G, Siracusano R, Ingrassia M, Germanò E, Calabrò MP, **Spina E**, Gagliano A. Evaluation of acute cardiovascular effects of immediate-release methylphenidate in children and adolescents with Attention Deficit Hyperactivity Disorder. *Neuropsychiatr Dis Treat* 2015; 11: 1169-1174.
200. Sultana J, **Spina E**, Trifirò G. Antidepressant use in the elderly: the role of pharmacodynamics and pharmacokinetics in drug safety. *Exp Opin Drug Metab Toxicol* 2015; 11: 883-892.
201. Morabito P, Miroddi M, Giovinazzo S, **Spina E**, Calapai G. Serenoa repens as an endocrine disruptor in a 10-year-old young girl: a new case report. *Pharmacology* 2015; 96(1-2):41-43.
202. Italiano D, Bruno A, Santoro V, Lanza G, Muscatello MR, Zoccali R, **Spina E**. Generic olanzapine substitution in patients with schizophrenia: assessment of serum concentrations and therapeutic response after switching. *Ther Drug Monit* 2015; 37: 827-830.
203. Bruno A, Morabito P, **Spina E**, Muscatello MR. The role of levomilnacipran in the management of depressive disorder: a comprehensive review. *Curr Neuropharmacol* 2016; 14: 191-199.
204. de Leon J, **Spina E**. What is needed to incorporate clinical pharmacogenetic tests into the practice of psychopharmacotherapy? *Exp Rev Clin Pharmacol* 2016; 9: 351-354.
205. Laganà AS, S'Amico V, Cartella SM, Sofo V, Salmeri FM, Triolo O, Bokal EV, **Spina E**. Management of women with epilepsy: from preconception to post partum. *Arch Gynecol Obstet* 2016; 293: 493-503.
206. Italiano D, Striano P, Russo E, Leo A, **Spina E**, Zara F, Striano S, Gambardella A, Labate A, Gasparini S, Lamberti M, De Sarro G, Aguglia U, Ferlazzo E. Genetics of reflex seizures and epilepsies in humans and animals. *Epilepsy Res* 2016; 121: 47-54.
207. Gasparini S, Ferlazzo E, Giussani G, Italiano D, Cianci V, Sueri C, **Spina E**, Beghi E, Aguglia U. Rapid versus slow withdrawal of antiepileptic monotherapy in 2-year seizure-free adult patients with epilepsy (RASLOW) study: a pragmatic multicentre, prospective, randomized, controlled study. *Neurol Sci* 2016; 37: 579-583.
208. **Spina E**, Hiemke C, de Leon J. Assessing drug-drug interactions through therapeutic drug monitoring when administering oral second-generation antipsychotics. *Exp Opin Drug Metab Toxicol* 2016; 12: 407-422.
209. **Spina E**, Pisani F, de Leon J. Clinically significant pharmacokinetic drug interactions of antiepileptics with new antidepressants and new antipsychotics. *Pharmacol Res* 2016; 106: 72-86.
210. Scuruchi M, D'Ascola A, Avenoso A, Campana S, Abusamra YA, **Spina E**, Calatroni A, Campo GM, Campo S. 6-mer hyaluronan oligosaccharides modulate neuroinflammation and alpha synuclein expression in neuron-like SH-SY5Y cells. *J Cell Biochem* 2016; 117: 2835-2843.
211. Lamberti M, Siracusano R, Italiano D, Alosi N, Cucinotta F, Di Rosa G, Germanò E, **Spina E**, Gagliano A. Head-to-head comparison of aripiprazole and risperidone in the treatment of ADHD symptoms in children with autistic spectrum disorder and ADHD: a pilot, open-label, randomized controlled study. *Pediatric Drugs* 2016; 18: 319-329.
212. Fabbri C, Crisafulli C, Calabrò M, **Spina E**, Serretti A. Progress and prospects in pharmacogenetics of antidepressant drugs. *Exp Opin Drug Metab Toxicol* 2016; 12: 1157-1168.
213. Sultana J, Fontana A, Giorgianni F, Pasqua A, Cricelli C, **Spina E**, Gambassi G, Ivanovic J, Ferrajolo C, Molokhia M, Ballard C, Sharp S, Sturkenboom M, Trifirò G. The effect of safety

- warnings on antipsychotic drug prescribing in elderly persons with dementia in the United Kingdom and Italy: a population-based study. *CNS Drugs* 2016; 30: 1097-1109.
- 214.Fagiolini A, Rocca, De Giorgi, **Spina E**, Amodeo G, Amore M. Clinical trial methodology to assess the efficacy/effectiveness of long-acting antipsychotics: randomized controlled trials vs naturalistic studies. *Psychiatry Res* 2017; 247: 257-264.
- 215.Caraci F, Sultana J, Drago F, **Spina E**. Clinically relevant drug interactions with anti-Alzheimer's drugs. *CNS & Neurological Disorders - Drug Targets* 2017; 16: 501-513.
- 216.Bruno A, Pandolfo G, Crucitti M, Cacciola M, Santoro V, **Spina E**, Zoccali R, Muscatello MRA. Low-dose of bergamot-derived polyphenolic fraction (BPF) did not improve metabolic parameter in second generation antipsychotics-treated patients: results from a 60-days open-label study. *Front Pharmacol* 2017; 8: 197.
- 217.Schoresanitis G, **Spina E**, Hiemke C, de Leon J, „A systematic review and combined analysis of therapeutic drug monitoring studies for long-acting risperidone. *Exp Rev Clin Pharmacol* 2017; 10; 965-981.
- 218.**Spina E**, de Leon J. Potentially clinically relevant pharmacodynamic drug interactions between antiepileptic drugs and psychotropic drugs: an update. *Clin Pharm Des* 2017; 23: 5625-5638.
- 219.de Leon J, **Spina E**. Possible pharmacodynamic and pharmacokinetic drug-drug interactions that are likely to be clinically relevant and/or frequent in bipolar disorder. *Curr Psychiatr Rep* 2018; 20: 17.
- 220.Muscatello MRA, Pandolfo G, Bruno A, Crucitti M, Troili GM, **Spina E**, Zoccali R. Red Yeast Rice (RYM) supplementation in patients treated with second-generation antipsychotics. *Compl Ther Med* 2018; 37: 167-171.
- 221.Formica D, Sultana J, Cutroneo PM, Lucchesi S, Angelica R, Crisafulli S, Ingrasciotta Y, Salvo F, **Spina E**, Trifirò G. The economic burden of preventable adverse drug reactions: a systematic review of observational studies. *Expert Opin Drug Saf* 2018; 17:681-695..
- 222.Giardina C, Cutroneo PM, Mocciano E, Russo GT, Mandraffino G, Basile G, Rapisarda F, Ferrara R, **Spina E**, Arcoraci V. Adverse drug reactions in hospitalized patients: results of the FORWARD (Facilitation of reporting in hospital Ward) study. *Front Pharmacol* 2018; 9: 308.
- 223.Marcianò I, Randazzo MP, Panagia P, Intelisano R, Sgroi C, Ientile V, Cannavò S, Guarneri C, Reitano P, **Spina E**, Trifirò G. Real world use of biological drugs in patients with psoriasis/psoriatic arthritis: a retrospective, population-based study from Southern Italy in the years 2010-2014. *G Ital Dermatol Venereol* 2018.
- 224.Schoresanitis G, **Spina E**, Hiemke C, de Leon J. A systematic review and combined analysis of therapeutic drug monitoring studies for oral paliperidone. *Exp Rev Clin Pharmacol* 2018; 11: 625-639.
- 225.Trifirò G, Marcianò I, Cutroneo PM, **Spina E**, Mirabelli E, Trombetta CJ, Morgante F. Long-term intravitreal ranibizumab as a potential additional risk factor for neurodegeneration in Parkinson's disease: a case report. *Front Pharmacol* 2018; 9: 608.
- 226.Brinkman DJ, Tichelaar J, Mookink LB, Christiaens T, Likic R, Maciulaitis R, Costa J, Sanz EJ, Maxwell SR, Richir MC, van Agtmael MA; Education Working Group of the European Association for Clinical Pharmacology and Therapeutics (EACPT) and its affiliated Network of Teachers in Pharmacotherapy (NOTIP). Key Learning Outcomes for Clinical Pharmacology and Therapeutics Education in Europe: A Modified Delphi Study. *Clin Pharmacol Ther* 2018;104: 317-325.
- 227.Fiorillo A, Carpinello B, De Giorgi S, La Pia S, Maina G, Sampogna G, **Spina E**, Tortorella A, Vita A. Assessment and management of cognitive and psychosocial dysfunctions in patients with major depressive disorder: a clinical review. *Frontiers in Psychiatry* 2018, Oct 11;9:493
- 228.Scavone C, Sessa M, Clementi E, Corrao G, Leone R, Mugelli A, Rossi F, **Spina E**, Capuano A. Real world data on the utilization pattern and safety profile of infliximab originator versus biosimilars in Italy: a multiregional study. *BioDrugs* 2018; 32: 607-617.

- 229.Schoretsanitis G, **Spina E**, Hiemke C, de Leon J. A systematic review and combined analysis of therapeutic drug monitoring studies for long-acting paliperidone. *Exp Rev Clin Pharmacol* 2018; 11: 1237-1253.
- 230.Cicala G, Barbieri MA, **Spina E**, de Leon J. A comprehensive review of swallowing difficulties and dysphagia in adults associated with antipsychotics. *Exp Rev Clin Pharmacol* 2019; 12: 219-234.
- 231.Ruan CJ, Zang YN, Wang CY, Cheng YH, Sun C, **Spina E**, de Leon J. Clozapine metabolism in East Asians and Caucasians: A pilot exploration of the prevalence of poor metabolizers and a systematic review. *J Clin Psychopharmacol* 2019; 39:135-144.
- 232.D'Angelo G, Granese R, Marseglia L, Impellizzeri P, Alibrandi A, Palmara A, La Rosa MA, Manti S, Salpietro C, **Spina E**, Reiter RJ, Falsaperla R, Corsello G, Gitto E. High mobility group box 1 and markers of oxidative stress in human cord blood. *Pediatr Int.* 2019; 61: 264-270.
- 233.Lo Giudice I, Mocciaro E, Giardina C, Barbieri MA, Cicala G, Giofrè-Florio M, Carpinteri G, Di Grande A, **Spina E**, Arcoraci V, Cutroneo PM. Characterization and preventability of adverse drug events as cause of emergency department visits: a prospective 1-year observational study. *BMC Pharmacology and Toxicology* 2019 Apr 27;20(1):21.
- 234.Schoretsanitis G, Kane JM, Ruan CJ, **Spina E**, Hiemke C, de Leon J. A comprehensive review of the clinical utility of and a combined analysis of the clozapine/norclozapine ratio in therapeutic drug monitoring for adult patients. *Exp Rev Clin Pharmacol* 2019; 12: 603-621.
- 235.Barbieri MA, Cicala G, Cutroneo PM, Mocciaro E, Sottosanti L, Freni F, Galletti F, Arcoraci V, **Spina E**. Ototoxic adverse drug reactions: a disproportionality analysis using the Italian spontaneous reporting database *Front Pharmacol* 2019 Oct 8;10:1161.
- 236.Muscatello MRA, Zoccali R, Pandolfo G, Mangano P, Lorusso S, Cedro C, Battaglia F, **Spina E**, Bruno A. Duloxetine in psychiatric disorders: expansions beyond major depression and generalized anxiety disorders. *Front Psychiatry* 2019 Oct 25;10:772.
- 237.Palleria C, Roberti R, Iannone LF, Tallarico M, Barbieri MA, Vero A, Manti A, De Sarro GB, **Spina E**, Russo E. Clinically relevant drug interactions between statins and antidepressants. *J Clin Pharm Ther* 2020; 45: 227-239..
- 238.**Spina E**, Barbieri MA, Cicala G, Bruno A, de Leon J. Clinically relevant drug interactions between newer antidepressants and oral anticoagulants. *Exp Opin Drug Metab Toxicol* 2020; 16: 31-44.
- 239.Cicala G, Barbieri MA, Santoro V, Tata C, Colucci PV, Vanadia F, Drago F, Russo C, Cutroneo PM, Gagliano A, **Spina E**, Germanò E. Safety and tolerability of antipsychotic drugs in paediatric patients: data from a 1-year naturalistic study. *Front Psychiatry* 2020 Mar 24; 11: 152.
- 240.Barbieri MA, Cicala G, Cutroneo MP, Gerratana E, Palleria C, De Sarro C, Vero A, Iannone L, Manti A, Russo E, De Sarro G, Atzeni F, **Spina E**. Safety profile of biologics used in rheumatology: an Italian prospective pharmacovigilance study. *J Clin Med* 2020, 9 1227; doi:10.3390/jcm9041227.
- 241.Bruno A, Zoccali RA, Troili GM, Scala L, Pandolfo G, Cedro C, Mento C, Santoro V, **Spina E**, Muscatello MRA. Vortioxetine on cognition in schizophrenia: a pilot study. *J Clin Psychopharmacol* 2020; 40: 381-385.
- 242.Roberti R, Iannone LF, Palleria C, De Sarro C, Spagnuolo R, Barbieri MA, Vero A, Manti A, Pisana V, Fries W, Trifirò G, Naturale MD, Larussa T, De Francesco AE, Bosco V, Donato di Paola E, Citraro R, Luzzo F, Bennardo L, Rodinò S, Doldo P, **Spina E**, Russo E, De Sarro GB. Safety profiles of biologic agents for inflammatory bowel diseases: a prospective pharmacovigilance study in Southern Italy. *Curr Med Res Opin* 2020; 36:1457-1463.
- 243.Cutroneo PM, Isgrò V, Ientile V, Santarpia M, Ferlazzo G, Matarangolo E, **Spina E**, Trifirò G. Safety profile of immune checkpoint inhibitors: an analysis of Italian Spontaneous Reporting System. *Br J Clin Pharmacol* 2021; 87:527-541 doi: 10.1111/bcp.14413



244. **Spina E**, Barbieri MA, Cicala G, de Leon J. Clinically relevant interactions between atypical antipsychotics and anti-infective agents. *Pharmaceuticals* 2020; 13: 439.
245. Schoretsanitis G, Smith RL, Molden E, Solismaa A, Seppala N, Kopecek M, Svancer P, Olmos I, Vázquez M, Iglesias-Garcia C, Iglesias-Alonso A, **Spina E**, de Leon J. European Whites may need lower minimum therapeutic clozapine doses than those customarily proposed. *J Clin Psychopharmacol* 2021; 41: 140-147.
246. Schoretsanitis G, Ruan CJ, Rhode C, Verdoux H, De Las Cuevas C, **Spina E**, de Leon J. An update on the complex relationship between clozapine and pneumonia. *Exp Rev Clin Pharmacol* 2021; 14:2, 145-149.
247. Barbieri MA, Cutroneo PM, Baratelli C, Cicala G, Battaglia A, Santoro V, Andò G, **Spina E**. Adverse drug reactions with oral anticoagulants: data from sicilian spontaneous reporting system database. *J Clin Pharm Ther.* 2021; 4: 1027-1040.
248. Franco V, Barbieri MA, Cutroneo PM, Arena I, Cicala G, Marchione P, **Spina E**, Perucca E. Pediatric adverse reactions to antiseizure medications – An analysis of data from the Italian Spontaneous Reporting System (2001– 2019). *Epilepsy & Behavior* 2021 Jun; 119: 107989.
249. Eap CB, Gründer G, Baumann P, Ansermot N, Conca A, Corruble E, Crettol S, Dahl ML, de Leon J, Greiner C, Howes O, Kim E, Lanzenberger R, Meyer JH, Moessner R, Mulder H, Müller DJ, Reis M, Riederer P, Ruhe HG, Spigset O, **Spina E**, Stegman B, Steimer W, Stingl J, Suzen S, Uchida H, Unterecker S, Vandenberghe F, Hiemke C. Tools for optimising pharmacotherapy in psychiatry (therapeutic drug monitoring, molecular brain imaging and pharmacogenetic tests): focus on antidepressants. *World J Biol Psychiatry.* 2021 22:561-628.
250. Crisafulli S, Cutroneo PM, Verhamme K, Ferrajolo C, Ficarra V, Sottosanti L, Di Giovanni V, **Spina E**, Trifirò G. Drug-induced urinary retention: an analysis of a national spontaneous adverse drug reaction reporting database. *Eur Urol Focus* 2021
251. de Leon, Schoretsanitis G, ... **Spina E**, ... An international adult guideline for making clozapine titration safer by using 6 ancestry-based personalized dosing titrations, CRP and clozapine levels. *Pharmacopsychiatry*, 2021
252. Minelli A, Barlati S, Vitali E, Bignotti S, Dattilo V, Tura GB, Maffioletti E, Giacomuzzi E, Santoro V, Perusi G, Cobelli C, Magri S, Bonizzato S, Bocchio-Chiavetto L, **Spina E**, Vita A, Gennarelli M. Clinical validation of a combinatorial PharmAcogeNomic approach in major Depressive disorder: an Observational prospective RANdomized, participant and rater-blinded, controlled trial (PANDORA trial). *Trials* 2021 Dec 11;22(1):896.
253. Barbieri MA, Sorbara E, Cicala, G, Santoro V, Cutroneo PM, Franchina T, **Spina E**. Adverse drug reactions with HER2-positive breast cancer treatment: an analysis from the Italian pharmacovigilance database. *Drugs – Real World Outcomes* 2022; 9: 91-107
254. Vaccaro M, Bertino L, Squeri R, Genovese C, Isola S, Spatari G, **Spina E**, Cutroneo P. Early atypical injection-site reactions to COVID-19 vaccine: a case series. *J Eur Acad Derm Venereol*, 2022; 36: e24-e26.
255. Dipasquale V, Cicala G, Laganà F, Cutroneo P, Felicetti P, Potenza S, Trimarchi G, **Spina E**, Romano C. Adverse reactions related to proton pump inhibitors in pediatric population: an analysis of spontaneous reporting data. *Exp Opin Drug Saf* 2022; 21: 127-132
256. Barbieri MA, Perucca E, **Spina E**, Rota P, Franco V. Cenobamate: A review of its pharmacological properties, clinical efficacy and tolerability profile in the treatment of epilepsy. *CNS & Neurol Disord-Drug Targets* (in press).
257. Barbieri MA, Sorbara E, Battaglia A, Cicala G, Rizzo V, **Spina E**, Cutroneo PM. Adverse drug reactions with drugs used in multiple sclerosis: an Analysis from the Italian Pharmacovigilance Database. *Front Pharmacol* (in press).
258. Dipasquale V, Cicala G, **Spina E**, Romano C. A narrative review on efficacy and safety of proton pump inhibitors in children. *Front Pharmacol – Obstetrics and Pediatric Pharmacol* (in press).

259. Dipasquale V, Cicala G, **Spina E**, Romano C. Biosimilars in pediatric inflammatory bowel diseases: a systematic review and real life-based evidence. *Front Pharmacol – Obstetrics and Pediatric Pharmacol* (in press).
260. McGrane I, **Spina E**, Hiemke C, de Leon J. Pharmacokinetic drug interactions with oral haloperidol in adults: dose correction factors from a combined weighted analysis *Exp Opin Drug Metab Toxicol* 2022; 18: 135-149.
261. De Filippis R, Kane JM, Kuzo N, **Spina E**, De Sarro GB, de Leon J, De Fazio P, Schoretsanitis G. Screening the European pharmacovigilance database for reports of clozapine-related DRESS syndrome: 47 novel cases. *Eur Neuropsychofarmacol* (in press).
262. Pisani F, Pisani RL, Barbieri MA, de Leon J, **Spina E**. Optimization of therapy in patients with epilepsy and psychiatric comorbidities: key points. *Curr Neuropharmacol* (in press)

## LIBRI

1. Schwaab M, Kaschka WP, **Spina E**. *Pharmacogenomics in Psychiatry*. Adv Biol Psychiatry, Basel, Karger, 2010.
2. **Spina E**, Trifirò G. *Pharmacovigilance in Psychiatry*. Springer, Heidelberg, 2016.
3. Salomone S, Capuano A, **Spina E**. *Compendio di Farmacologia Generale e Speciale*. Edr, 2021.

## CAPITOLI DI LIBRI

1. von Bahr C, Astrom A, Birgersson C, Blanck A, Ericsson O, **Spina E**. Hydroxylation of desmethylimipramine and debrisoquine in human and rat liver in vitro. In: *Microsomes and Drug Oxidations*, edited by AR Boobis, J Caldwell, F De Matteis and CR Elcombe (Taylor & Francis, London and Philadelphia) pp 370-379, 1985.
2. **Spina E**. Hydroxylation of desmethylimipramine in man. In vivo and in vitro studies on the relationship to polymorphic debrisoquine oxidation. MD Thesis, Stockholm 1987.
3. **Spina E**, Steiner E, Dumont E, Dahlqvist R. Inhibition of desipramine 2-hydroxylation by quinidine and quinine in rapid and slow debrisoquine hydroxylators. In: *Clinical Pharmacology in Psychiatry*. Eds: S.G. Dahl and L.F. Gram. Springer-Verlag Berlin Heidelberg, 201-205, 1989.
4. Caputi AP, **Spina E**. Interazioni tra farmaci. In: *Terapia nella pratica medica. Scelta e valutazione dei trattamenti*. Eds L Pagliaro, E Geraci. Ed. Medico-Scientifiche, Torino, 2563-2596, 1991.
5. **Spina E**, Caputi AP. Reazioni avverse da farmaci. In: *Terapia nella pratica medica. Scelta e valutazione dei trattamenti*. Eds L Pagliaro, E Geraci. Ed. Medico-Scientifiche, Torino, 2597-2636, 1991.
6. **Spina E**, Sjoqvist F. Amitriptyline (hydrochloride). In: *Therapeutic Drugs*. Vol I. Eds Sir Colin Dollery et al. Churchill Livingstone, Edinburgh, pp A95-A100, 1991.
7. **Spina E**, Caputi AP. Neuropsicofarmacologia geriatrica. In: *Neurogeriatria oggi*. Eds R Di Perri, V Nicita-Mauro, M Meduri. Editoriale Bios, Cosenza, pp. 63-76, 1993.
8. **Spina E**, Scordo MG, Avenoso A, Facciola G. Farmacologia degli inibitori selettivi della ricaptazione della serotonina. In: *Crisi, pseudocrisi e attacchi di panico*. Eds L Murri, A Iudice, GB Cassano. Springer, Milano, pp 209-220, 1998.
9. **Spina E**, Avenoso A, Facciola G, Fabrazzo M, Monteleone P, Maj M, Perucca E, Caputi AP. Interaction between fluoxetine and clozapine: pharmacokinetic and clinical implications. In: *Clinical pharmacology in psychiatry: finding the right dose of psychotropic drugs*. Eds LP Balant, J Benitez, SG Dahl, LF Gram, RM Pinder, WZ Potter. European Commission, Brussels, pp. 143-148, 1998.

10. **Spina E**, Perucca E. I parametri farmacocinetici: definizione, determinazione e rilevanza clinica. In: *Farmacologia Clinica*. Eds L Fuccella, E Perucca, C Sirtori. UTET, Torino, pp. 51-64, 1998.
11. Benitez J, Dahl ML, **Spina E**, Carrillo JA. Genetic and environmental factors causing variability in psychotropic drug response. In: *Interindividual variability in human drug metabolism*. Eds GM Pacifici, O Pelkonen. Taylor & Francis, London, pp. 85-128, 2001.
12. **Spina E**. Carbamazepine: chemistry, biotransformation, and pharmacokinetics. In: *Antiepileptic Drugs*, 5<sup>th</sup> Ed. by RH Levy, RH Mattson, BS Meldrum, and E Perucca. Lippincott Williams & Wilkins, Philadelphia, pp. 236-246, 2002.
13. **Spina E**, Scordo MG. Le interazioni farmacologiche degli psicofarmaci. In: *Trattato di psicofarmacologia clinica*. Ed. C. Bellantuono, M. Balestrieri. Il Pensiero Scientifico Editore, Roma, pp. 449-482, 2003.
14. **Spina E**, Scordo MG. Pharmacogenetics of Psychopharmacological Agents. 15th IFCC-FESCC European Congress of Clinical Chemistry Laboratory Medicine. Euromedlab 2003. Monduzzi Editore, pp. 137-142, 2003.
15. **Spina E**, Scordo MG. Drug Interactions in Epilepsy. In: *The Treatment of Epilepsy*, 2nd Ed. by S Shorvon, DR Fish, E Perucca, WE Dodson, A Olivier. Blackwell Science, Oxford, pp. 123-139, 2004.
16. **Spina E**, D'Arrigo C, Migliardi G. Interazioni farmacologiche dei nuovi antipsicotici. CIC Edizioni Internazionali, Roma, 2005.
17. **Spina E**, Perucca E, Levy R. Predictability of metabolic antiepileptic drug interactions. In: *Antiepileptic Drugs: Combination Therapy and Interactions*. Ed. by J Majkowski, BFD Bourgeois, PN Patsalos, RH Mattson. Cambridge University Press, Cambridge, pp. 57-92, 2005.
18. Trifirò G, **Spina E**, Savica R, Beghi E, Innocenti F, Mazzaglia G, Brignoli O, Cricelli C, Caputi AP. Prescribing pattern of anti-epileptic drugs in Italy: a population-based study. 8<sup>th</sup> Congress of the EACPT. Monduzzi Editore, pp. 43-46, 2007.
19. **Spina E**. Drug interactions. In: Shorvon S, Perucca E, Engel J, eds. *Treatment of Epilepsy*, 3rd ed. Oxford: Wiley-Blackwell Publishing Ltd, pp. 361-377, 2009.
20. Rabboni M, **Spina E**. Reazioni avverse psichiatriche. In *Reazioni avverse a farmaci: sospetto e diagnosi*. Eds. AP Caputi, F De Ponti, L Magliaro. Raffaello Cortina Editore, Milano, pp. 251-266, 2009.
21. Serretti A, Drago A, **Spina E**. Pharmacogenomics of depression. In: Schwaab M, Kaschka WP, Spina E (eds). *Pharmacogenomics in Psychiatry*. Adv Biol Psychiatry, Basel, Karger, pp. 58-74, 2010.
22. Italiano D, **Spina E**. New antiepileptic drugs. In: Patsalos P, ed. *Advances in Antiepileptic Drug Development*. Future Medicine, pp. 38-52, 2011.
23. **Spina E**, Italiano D. Drug interactions. In: Shorvon S, Perucca E, Engel J, eds. *Treatment of Epilepsy*, 4th ed. Oxford: Wiley-Blackwell Publishing Ltd pp. 191-207, 2015.
24. **Spina E**, Trifirò G, Caputi AP. Pharmacovigilance in psychiatry: an introduction. In: Spina E, Trifirò G, eds. *Pharmacovigilance in Psychiatry*. Springer, Heidelberg, pp. 3-7, 2016.
25. Arcoraci V, **Spina E**. Safety and tolerability of anxiolytics/sedative hypnotics. In: Spina E, Trifirò G, eds. *Pharmacovigilance in Psychiatry*. Springer, Heidelberg, pp. 191-207, 2016.
26. **Spina E**, Italiano D. Mood stabilizers. In: Jann MW, Penzak RS, Cohen LJ, eds. *Applied Clinical Pharmacokinetics and Pharmacodynamics of Psychopharmacological Agents*. Springer, Heidelberg, pp. 177-204, 2016.
27. Cicala G, Barbieri MA, **Spina E**. Disturbo depressivo maggiore. In: Calignano A, ed. *Manuale di Farmacoterapia*. Idelson-Gnocchi, Napoli, 739-754, 2019.
28. Barbieri MA, Cicala G, **Spina E**. Schizofrenia. In: Calignano A, ed. *Manuale di Farmacoterapia*. Idelson-Gnocchi, Napoli, 755-781, 2019.

Dichiaro che le informazioni riportate nel presente Curriculum Vitae sono esatte e veritiere.

Autorizzo il trattamento dei dati personali, ivi compresi quelli sensibili, ai sensi e per gli effetti del decreto legge 196/2003.

Messina, li 24 maggio 2022

Prof. Edoardo Spina

A handwritten signature in purple ink, appearing to read 'Edoardo Spina', written over the printed name.