

Blueberry anthocyanins in POCD prevention

A winning strategy for
neuroprotection



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Dipartimento Integrato Interistituzionale
DIPINT



Primo Workshop
Clinical Research and Innovation

Venerdì 4 luglio 2014 9.00 - 19.00
Aula Magna - Polo Fibonacci - Largo Pontecorvo 3, Pisa



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Post Operative Cognitive Dysfunction: Definition

Postoperative Cognitive Dysfunction (POCD) is a decline in cognitive function for weeks or months after surgery

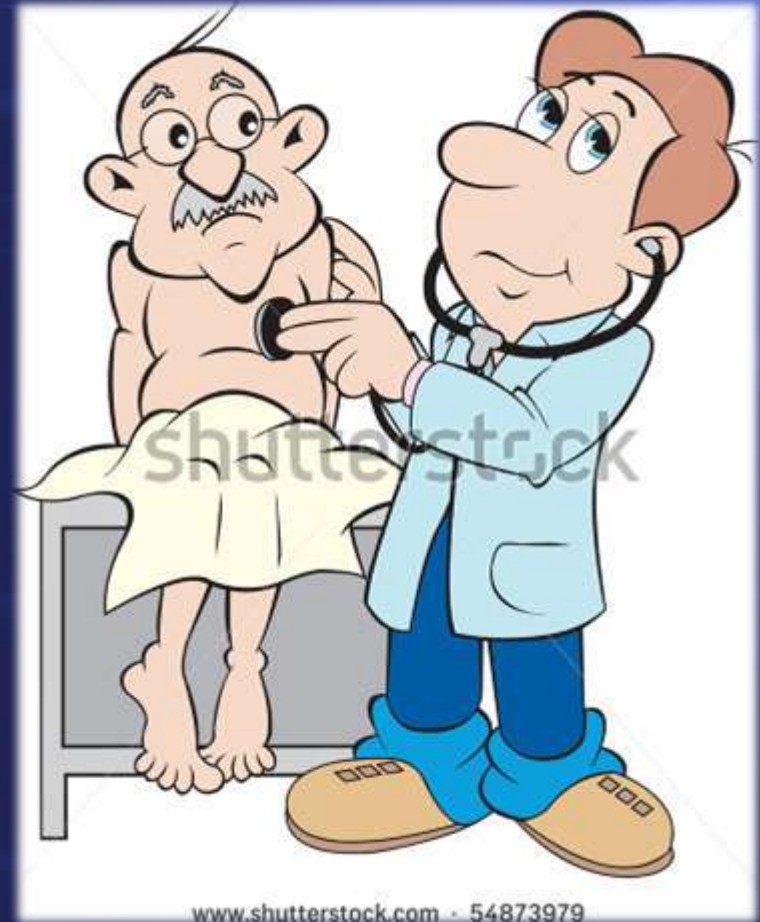
- Intellectual function deterioration manifested by a broad spectrum of symptoms, including loss of memory and concentration
- Possibility of subclinical forms



This may be a social burden!!!

POCD: incidence and risk factors

- Range between 19-41% one week after non cardiac surgery in pts > 18 years
- Association with a worse outcome
- Age (> 60 years) is the main risk factor



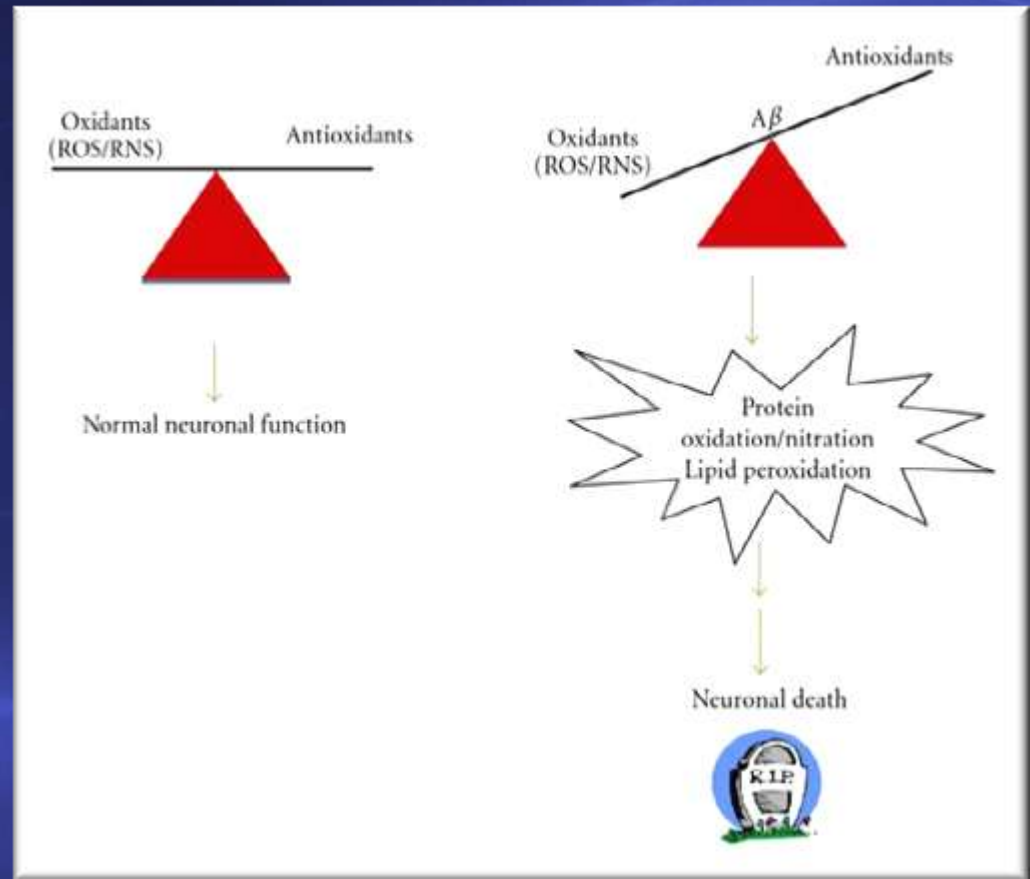
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Risk factors for postoperative cognitive dysfunction (POCD)

Risk factors	
Patient	advanced age; pre-existing cerebral, cardiac, or vascular disease; preoperative mild cognitive impairment (MCI); low educational level; history of alcohol abuse
Operation	extensive surgical procedure, intra- or postoperative complications, secondary surgery
Anesthesia	long-acting anesthetic, marked disturbance of homeostasis, organ ischemia due to hypoxia and hypoperfusion, intra- or postoperative anesthesiological complications

General anesthetics & oxidative stress

- General anesthetics induce oxidative stress and are pro-inflammatory
- They favor beta-amyloid accumulation



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Anesthesia, Surgery May Double Dementia Risk

Megan Brooks

March 11, 2014

Blueberry Polyphenols and Neuroprotection

*Marilù Giacalone, Filippo Di Sacco, Ippolito Traupe, Nicola Pagnucci,
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TABLE 2.1 Summary of Molecular and Behavioral Effects of Blueberry Polyphenols

Molecular Effects	Mechanisms	Behavioral Effects
Decreased damage related to oxidative stress	Direct scavenging activity, enhancement of endogenous antioxidant, reduced production of ROS	Improvement of long- and short-term memory, working memory, anxiety-related behavior, locomotion activity, and exploratory behavior in young animals
Counteraction of β -amyloid toxicity	Oxidative stress suppression, normalization of stress response, hormesis, restoration of ATP availability	Improvement of spatial memory and reversal learning in young animals
Antiamyloidogenic	Reduced production and increased clearance of β -amyloid	Reversal of deficits in spatial and working memory, object-recognition memory, and motor performance in aged animals
Antiinflammatory	Suppression of oxidative stress, reduced expression of proinflammatory cytokines	Amelioration of memory performance and processing speed, possible improvement of mood in humans
Antiexcitotoxic	To be determined	
Normalization of sensitivity to neurotransmitters	Improvement of oxidative stress signaling and calcium homeostasis	
Enhancement of synaptic plasticity and cell survival	Normalization of LTP, increased hippocampal neurogenesis and levels of growth factors, gene expression related to cell viability, genoprotection	

Several mechanisms are involved in blueberry-mediated neuroprotection, with influences on both cognitive and motor performances. ROS, reactive oxygen species; ATP, adenosine-triphosphate; LTP, long-term potentiation.

A study in humans...

- 9 persons with physiological age-related decline
- Daily assumption of BB juice for 12 weeks (6-9 ml/Kg) divided into the 3 main meals (treatment and placebo)
- Memory function improved in the treated subjects



Blueberry Supplementation Improves Memory in Older Adults[†]

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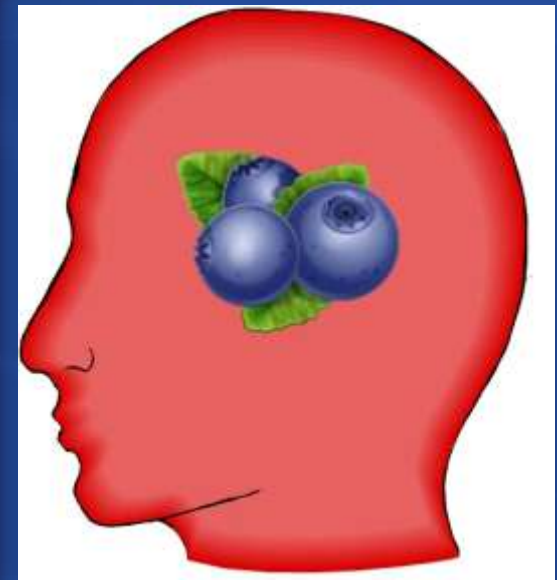
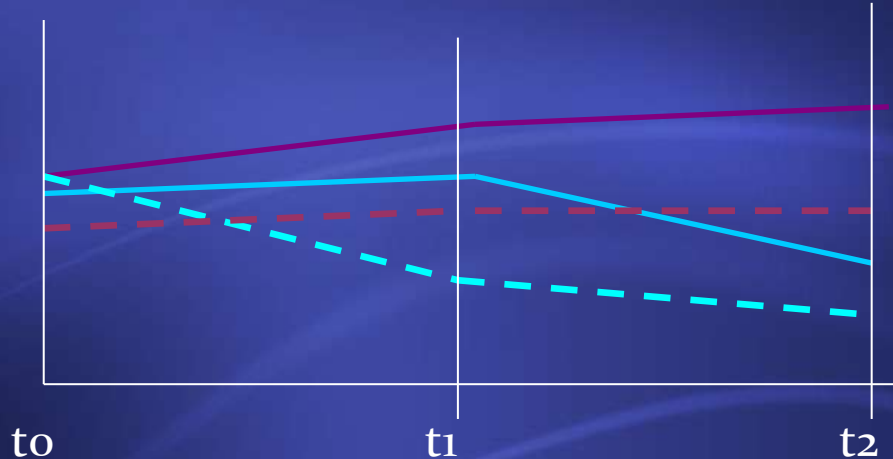


Pilot study involving UO IV Anestesia and Rianimazione of University of Pisa conducted on 26 patients, of which 13 were treated and 13 were controls, who had assumed 500 ml of blueberry juice within 2 weeks before the surgery

Memoria di Prosa ($F=4.82$, $dof=2$, $p=0,011$)

Trial Making Test B ($F=5.6$, $dof=2$, $p: 0,005$)

—



Vincoli derivanti da rapporti contrattuali con soggetti terzi

(indicare il tipo di contratto e le clausole sulla proprietà intellettuale in esso previste)

nessun vincolo con fornitori del prodotto alimentare.....

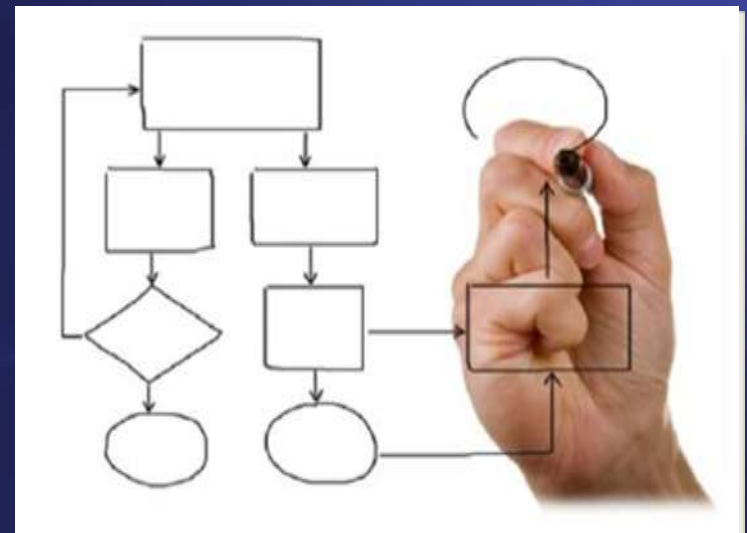
Titolo dell'invenzione

USO DI SUCCO DI MIRTILLO PER LA PROTEZIONE DEL S.N.C. NELLE FASI
PERIOPERATORIE DEL PAZIENTE ANZIANO

BIPOCID PROJECT

- **Blueberry in Post-Operative Cognitive Dysfunction**

- 150 PATIENTS
- MAJOR GENERAL SURGERY
- PLACEBO GROUP
- SELECTED NEUROPSYCHOLOGICAL TEST
- INTRA-OPERATIVE CEREBRAL OXIMETRY (NIRS)
- INTRA-OPERATIVE CARDIAC OUTPUT MONITORING
- BLOOD TEST (INFLAMMATION, OXIDATIVE STRESS, NEUROLOGICAL DAMAGE)
- BLUEBERRY ESSENCE



Take Home Message

- POCD is a frequent and underdiagnosed problem
- Any surgical procedure—even a minor outpatient operation—is associated with risk
- Age is the most important risk factor
- Anesthesia may exert oxidative stress and neuronal damage
- Blueberry are among the richest in flavonoids content
- Increasing evidences of neuroprotective effects in human
- Pre-operative administration is beneficial



Thank you



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POCD: pathogenesis

