

Esketamine and trauma-focused therapies

A key to exit the tunnel?



Docteur Philippe Raynaud de Prigny



PTSD, a debilitating condition

Life-time prevalence 7%

(Kessler et al, 2005)

One-third of patients remain symptomatic for up to 10 years

(Kessler et al, 1995)

Many comorbidities among them 50% MDD

(Rytwinski et al., 2013)

Trauma focused therapies seems efficient but.....

Accessibility issues

High drop-out rates (CBT)

Persistent symptoms

(Jonas et al., 2013)

Lack of efficacy for SSRI

(Ipser et al., 2012)

Medication-enhanced psychotherapy are innovative and promising

Three categories for PTSD

(Dunlop et al., 2012)

Cognitive enhancers

D-cyclosérine, Yohimbine fear extinction

Memory disrupters

Propranolol (Brunet et al., 2018) (Roullet et al., 2022)

Therapy facilitators

MDMA (Johansen et al., 2009) *oxytocin*

MDMA +PE (Latimer et al., 2021)

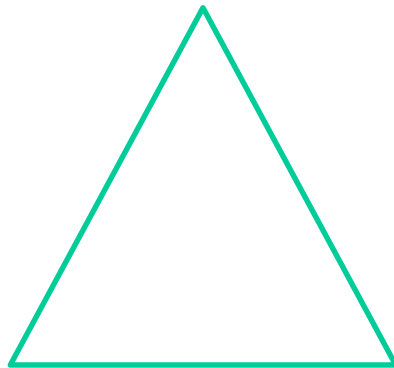
Esketamine (Artin et al., 2022) (Rothärmel et al., 2022) (Rothärmel et al., 2024)
(Roullet, Raynaud de Prigny et al., 2025)

Make dissociation great again!

Dissociation was a core explanation model of mental diseases for the alienists in XIX Century

Moskowitz et al., 2008

*Dissociation as an adaptative mechanism
of brain exposed to trauma*



*Dissociation as a lack of ability
to assess the reality
of internal experiences*

*Dissociation strongly correlated
with childhood trauma
(cumulative effect)*



Pierre Janet (1859-1947)

Granier C, 2022

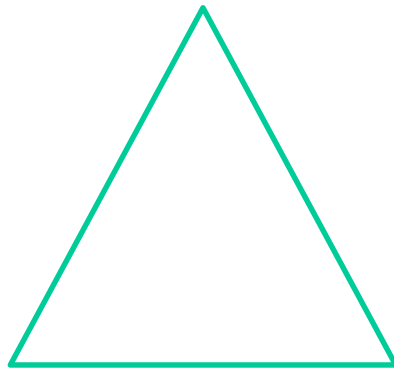
Wearne et al., 2020

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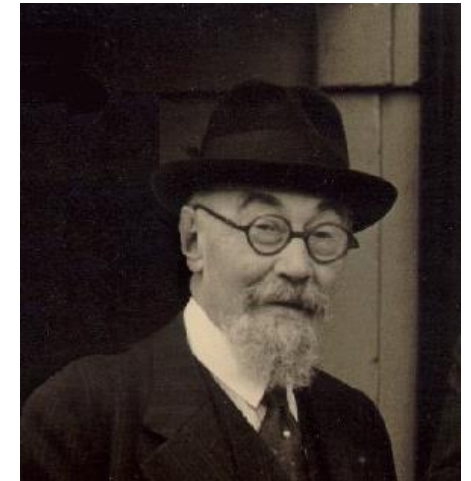
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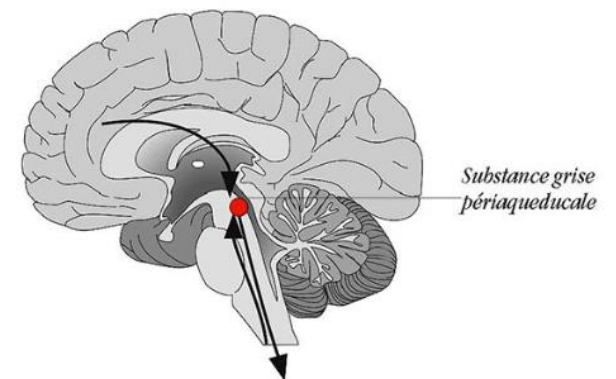
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What if therapy fails?



The best moment to use esketamine

EMDR Phases

Phase I



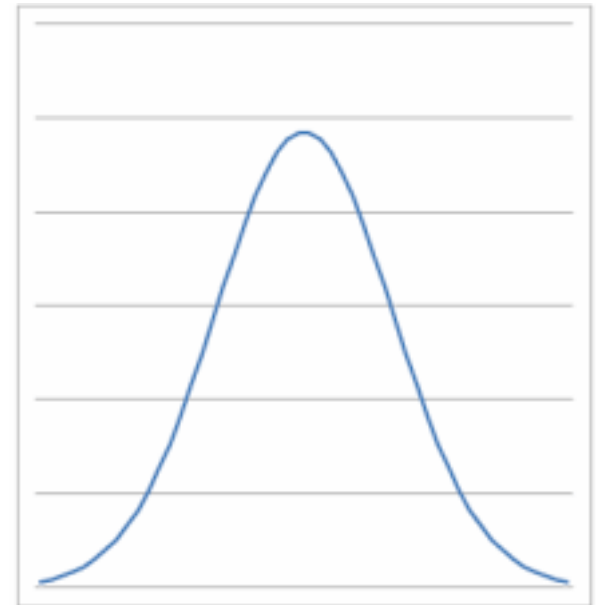
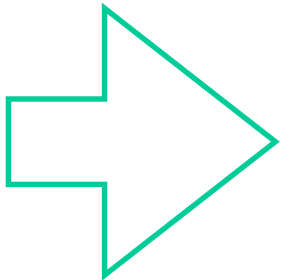
Phase II



Phase III



Phase IV



Peak at 40 mn



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Research Paper

Esketamine facilitate psychotherapies for Post-Traumatic stress disorder: A retrospective case series of six patients

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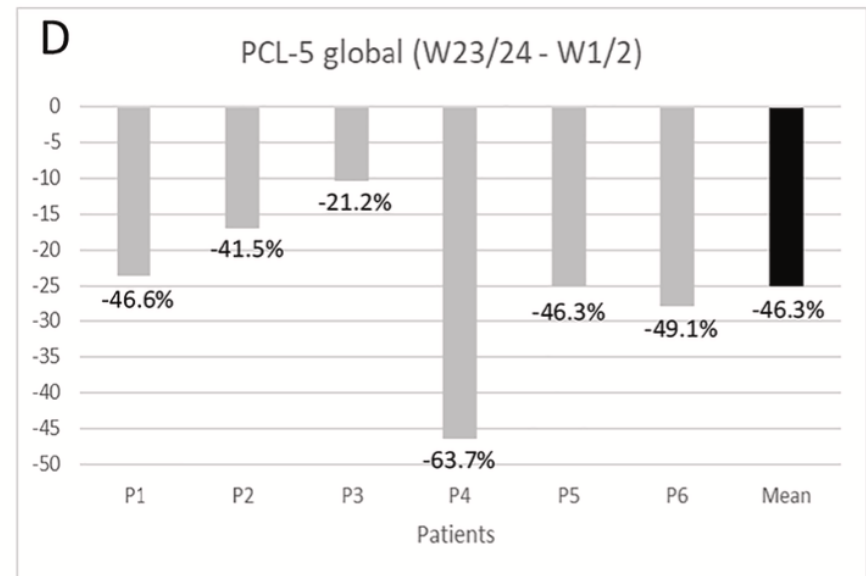
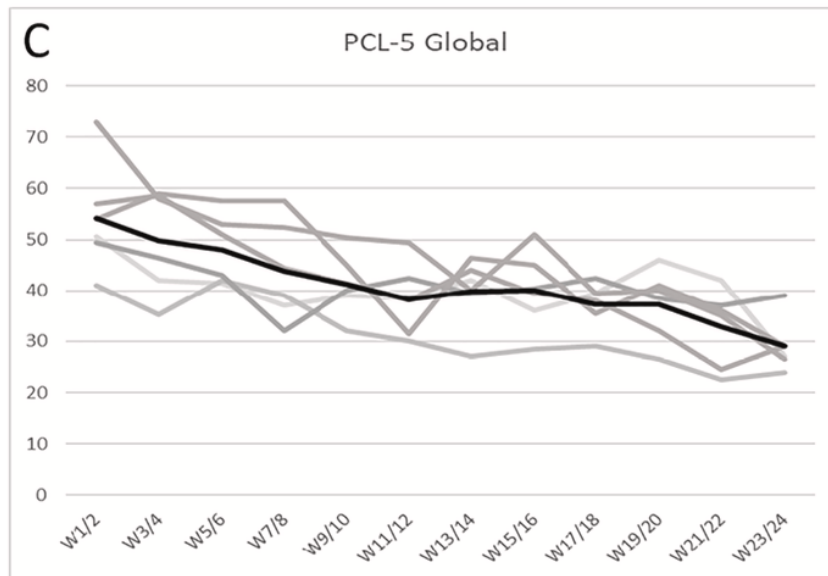
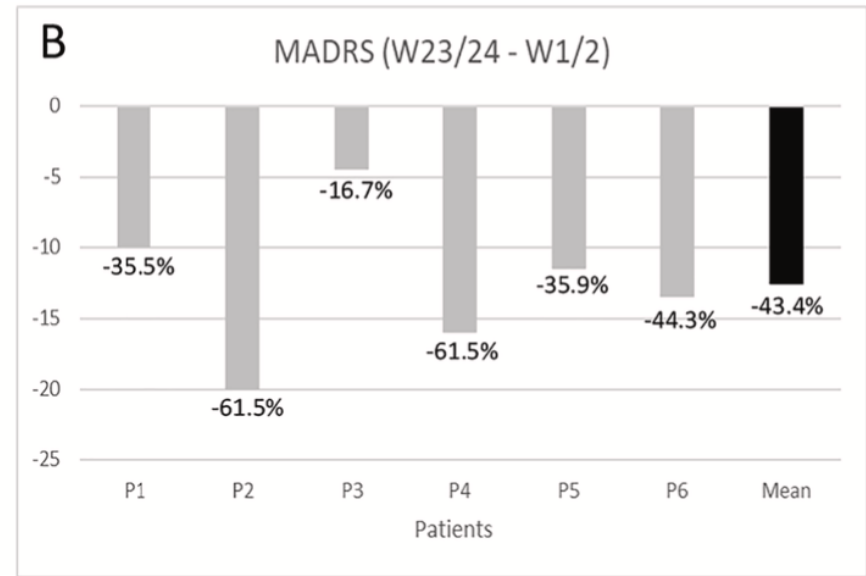
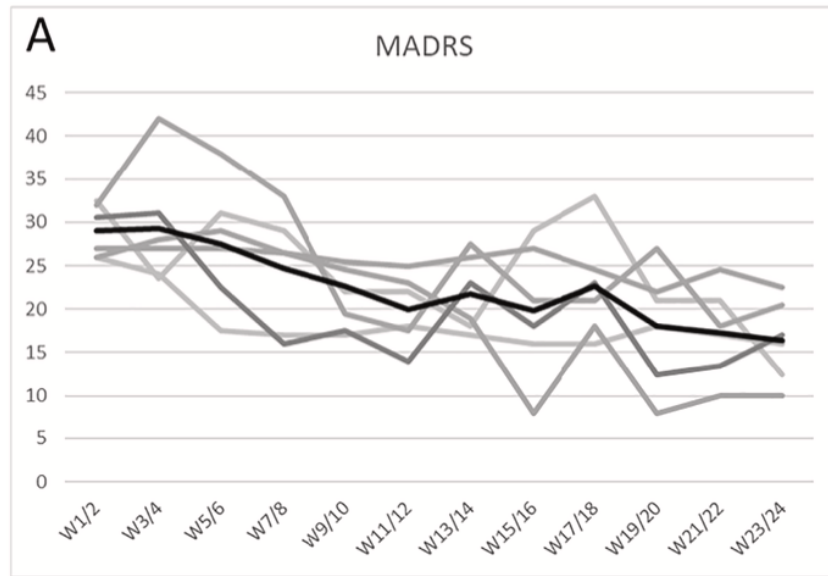


Fig. 1. On the 4 graphs, the values of the 6 patients are represented in gray and the average of these 6 patients in black. A: change of MADRS scores and B: change of PCL-5 global scores during the 24 weeks of the therapeutic procedure. B: change in MADRS scores and D change in PCL-5 scores for each patient between the start and end of the procedure (score W23/24 – score W1/W2). A negative value is therefore associated with a reduction in the score, meaning an improvement of the patient. The percentage in the Fig. represent the percentage reductions in MADRS scores in [Fig 1B](#), and the percentage reductions in PCL-5 scores in [Fig 1D](#) between the start and end of the procedure for each patient and for the average of the 6 patients. W= weeks P= Patients.

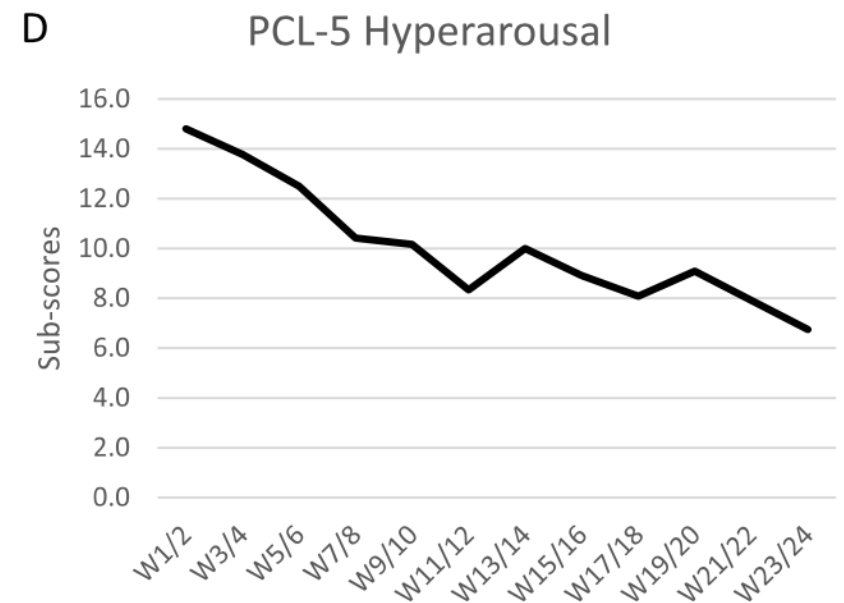
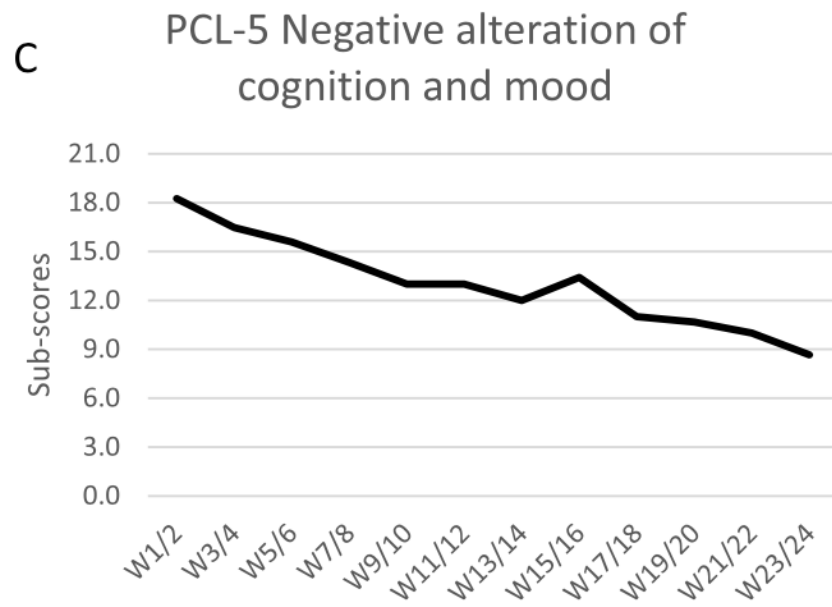
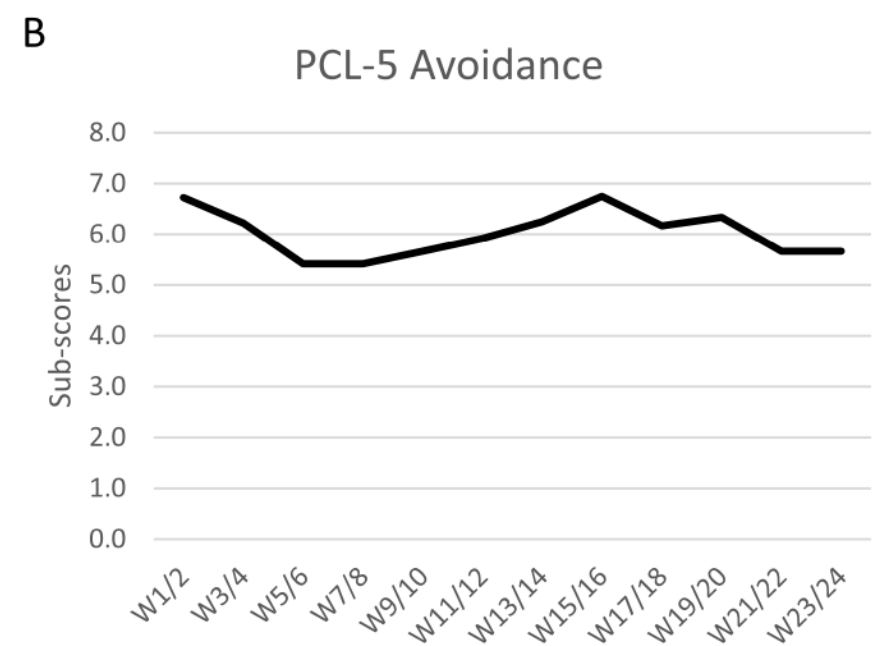
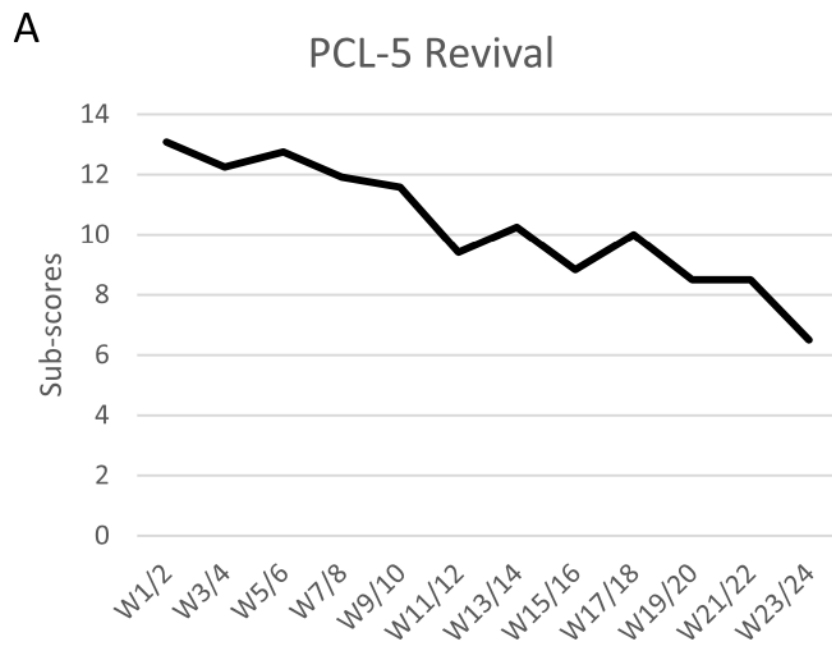


Fig. 2. changes of PCL-5 sub-scores (means) during the 24 weeks of the therapeutic procedure. A: re-experiencing sub-scores, B: avoidance sub-scores, C: negative alteration of cognition and mood sub-scores and D: hyperarousal sub-scores. W= weeks.

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ABSTRACT

Introduction: medication-enhanced psychotherapies are increasingly used to treat Post Traumatic Stress Disorder (PTSD). Esketamine, used in patients with treatment-resistant depression (TRD), sounds very promising as a new treatment for PTSD. Thus, our main objective was to investigate whether Esketamine associated with psychotherapy could reduce symptoms of both depression and PTSD in patients with complex PTSD.

Methods: We retrospectively collected clinical data of 6 patients receiving Esketamine nasal spray for TRD with comorbid PTSD. This treatment was always associated with a psychotherapy (supportive therapy, EMDR or hypnosis) and was prescribed twice then once per week during 24 weeks.

Results: During the different sessions, five patients exhibited a clear improvement in depression and the MADRS score decreased by an average of 12.6 points. For PTSD, all patients presented a clear reduction of their PCL-5 scores ranging from -10.5 to -46.5 points. Moreover, we observed that 3 different sub-scores of the PCL-5 (re-experiencing, negative alteration of cognition and mood and hyper arousal) decreased significantly during sessions, but it was not the case for the avoidance sub-score.

Discussion: Esketamine treatment associated with psychotherapies appears promising in patients with resistant complex PTSD and TRD. However, these encouraging results need to be confirmed in a standardized study with a larger sample size.

Thank you for your attention!

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