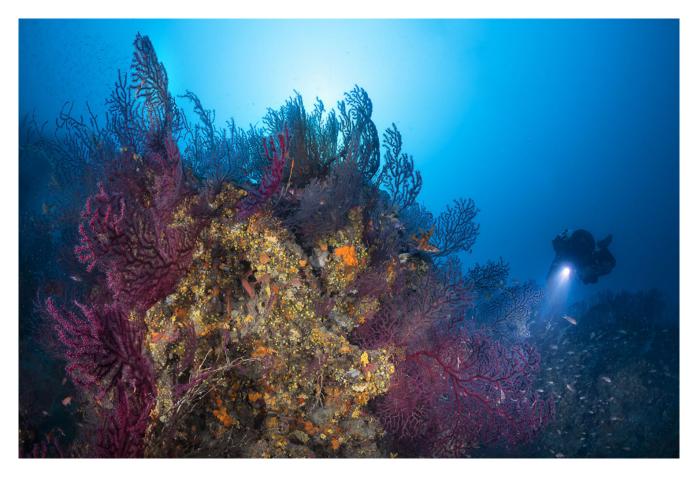
Measuring Inert Gas Narcosis

Though our understanding of the exact mechanisms and effects are still evolving, inert gas narcosis (IGN), which was poetically described as "l'ivresse des grandes profondeurs," or "rapture of the deep" by Jacques Cousteau in 1953, has long been recognized as a major risk factor that impacts diver safety and has been implicated in diving fatalities. Indeed, sport divers are much more likely to experience IGN than decompression illness (DCI), and though it's been shown that divers don't develop a tolerance for narcosis, they can learn to cope with it to varying degrees.

In the early days of scuba, nitrogen narcosis was the predominant limiting factor for dives beyond about 30-40 meters (m), and divers had to deal with increasing impairment, at their own peril, as they ventured deeper. Today, with the benefit of mixed gas technology, the operational risks of IGN can easily be mitigated.



However, there remains disagreement as to how much narcosis is tolerable, or prudent, to what extent it can, or should, be managed, and whether oxygen also contributes to the narcotic potency of a diver's breathing gas, which was first proposed by the National Oceanic and Atmospheric Administration (NOAA) in its 2002 diving manual. As a result, **practices vary widely among the sports diving community**.

A major challenge in studying IGN has been the lack of an objective, reliable measure to quantify the onset and severity of narcosis. Divers have proven unreliable in self-assessing subjective symptoms, and in addition, traditional psychological testing can be difficult to administer underwater, and motivation, experience and learning can influence results.

However, over the last decade, DAN Europe researchers have published a series of papers evaluating the results and efficacy of a new tool for assessing a diver's cognitive function called Critical Flicker Fusion

Frequency (CFFF), which promises to be an objective, reliable measure of IGN, that can be easily implemented in the field.

This article focuses on two papers which offer some surprising new insights into IGN. The first, published in 2016, <u>"Do Environmental Conditions Contribute to Narcosis Onset and Symptom Severity?</u>" examined the effects of different hyperbaric environments on IGN and concluded that pressure and gas may be the sole external factors influencing narcosis. It also found that onset of IGN begins after a brief period of heightened mental acuity upon descent, and its effects persist at least 30-minutes post dive.

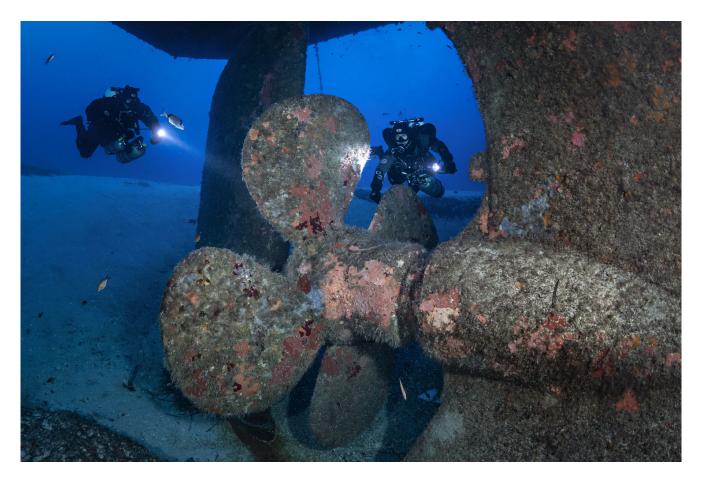
The second paper, "Early detection of diving-related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency," compared IGN for air and enriched air nitrox (EANx) dives using both CFFF and traditional psychological tests, and concluded that the elevated partial pressures of oxygen in EAN may offer a potent modulator of the effects of IGN.

The Skinny on Flicker Fusion

Critical Flicker Fusion Frequency (CFFF) is the frequency at which a flickering light is perceived as a steady

continuous light. First developed in the early 20th century for studying the physiology of vision, CFFF has become an important tool for measuring mental alertness and acuity under conditions involving pathology, anesthesia, and occupational exposures in aviation.

As a subjects' cognitive functions are impaired or diminish, the frequency at which they perceive the flickering to cease, i.e. the "fusion frequency," decreases. Conversely, in states of increased mental alertness, the fusion frequency increases. Since individuals perceive differing frequencies, a subject's baseline fusion frequency is considered 100%, and CFFF is measured as a percentage of baseline.



DAN USA founder, Dr. Peter Bennett first reported on the correlation between the mental states of divers, CFFF and electro-encephalogram (EEG) in 1960. More than a decade later, researchers found that CFFF changes during a deep 62 ATA oxygen-helium saturation dive were grossly parallel to changes in EEG. However, subsequent investigators were unable to replicate the results, and the use of CFFF was abandoned.

In recent years, at the suggestion of Maltese hyperbaric doctor Lyubisa "Luba" Matity, who is also a commercial and technical diver, DAN researchers resurrected the obscure measure and demonstrated promising results. They showed that CFFF tests give reliable measurements underwater (2012), and provided an assessment of a diver's cognitive function similar to some of the tests from the Psychology Experiment Building Language (PEBL), when breathing air and oxygen at atmospheric pressure (2014). They also found the results of the tests were consistent when breathing hyperbaric air and EANx 40% (40% O_2 , balance N_2).

CFFF tests are typically easier to administer underwater than PEBL testing, and arguably less easily influenced by the subject. The tests are conducted using a cylindrical, water-proof housing with a rotating ring containing a digital numeric frequency indicator with a transparent acrylic window, and a flexible cable connected to a single blue LED housed in a small cylindric container.



During the test, the diver looks straight into the LED at a comfortable distance. The investigator then increases or decreases the flicker frequency by rotating the ring. When the diver sees the LED change from flicker to fusion, or vice versa, the test is stopped, and the fusion frequency is recorded.

Typically, each subject performs the test three times, and the average is calculated and used for analysis. The results are compared divers' pre-dive CFFF, which serves as a baseline. In this case, an increase in fusion frequency was equated with brain activation while a decrease was considered evidence of IGN.

How Much Does Environment Matter?

Since divers adapt underwater, it is well recognized that the environment itself is likely to influence performance through a combination of factors. Accordingly, many factors have been put forward as

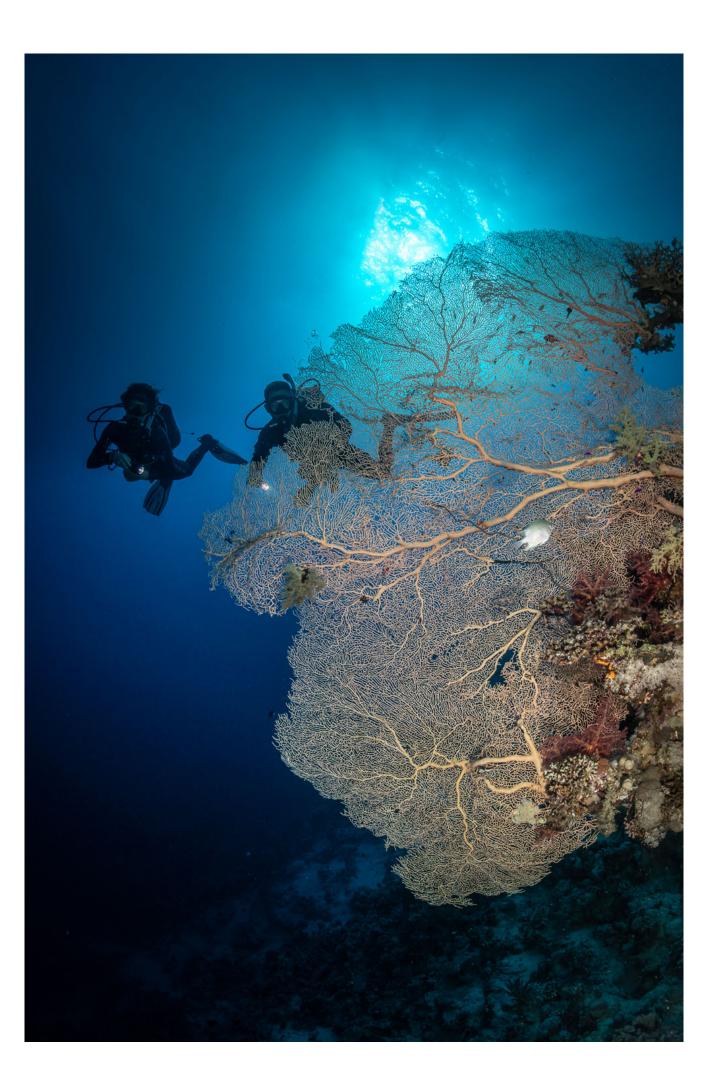
contributing to IGN onset and severity.

Firstly, elevated partial pressures of carbon dioxide (PCO_2) resulting from exertion due to work, heavy swimming, and also the work of breathing due to the inherent resistance in the breathing system, is a prime suspect. Elevated PCO_2 s are thought to enlarge cerebral blood vessels leading to higher nitrogen levels in the brain. Cold is also a likely factor, as it causes peripheral vessels to constrict, but since brain vessels cannot constrict, it results in an increased cerebral nitrogen load.

Other factors thought to contribute to IGN include alcohol and or drug use, a hangover or fatigue, anxiety, task loading, stress, restricted visibility, the rate of descent, vertigo and spatial disorientation. However, from a scientific viewpoint, the evidence has not been particularly strong for any these factors, and more data is needed. For that reason, this first study focused on the diving environment.

Weird (Wet) Science

Researchers wanted a relatively uniform group for the study and so recruited 40 non-smoking males aged 30-40, who exercised regularly and boasted a "healthy" Body Mass Index (BMI) of 20-25, from the sport diving community. Divers taking any medications were excluded. In addition, the divers refrained from alcohol 72-hours hours before the dives.



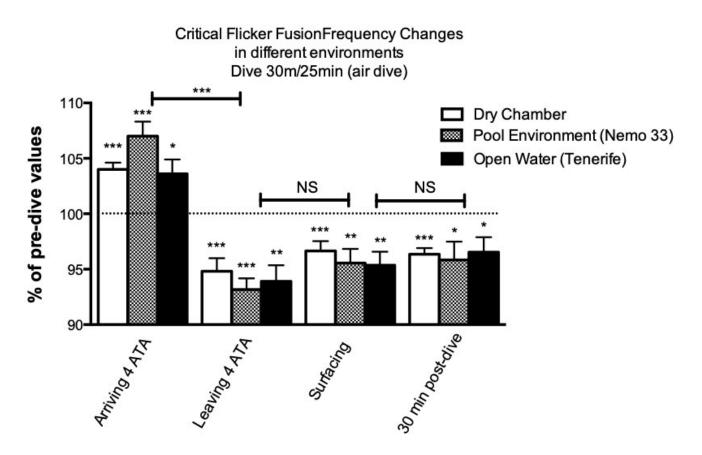
The test dives were conducted to 30m with 20-minute bottom times in three distinct environments; a hyperbaric chamber in Brussels, Belgium, the Nemo 33 pool also in Brussels, and an ocean dive in Tenerife, Spain. Though the dives did not require decompression, subjects conducted a single 5-minute safety stop at 5m. Descent speed: 15m/minute; ascent speed: 10m/minute.

Water temperature in the pool was 33°C, and no thermal protection required. Ocean temperature was 19°C, and divers wore an appropriate wet suit.

Five sets of CFFF measurements were taken for each dive. These were:

- Pre-dive to set divers' baselines
- Upon arriving at 30m depth
- Five-minutes before surfacing
- Upon surfacing
- Thirty-minutes post-dive

According to the authors, this is the first time that effects of IGN were measured in a standard population under different environmental conditions i.e. dry vs. wet, a protective suit vs. none, no "up" references in blue water vs. a pool). Their findings were surprising.



First, as shown in Figure 1, CFFF results for the dives were remarkably consistent for each of the three environments. First, divers' CFFF values increased upon arriving at depth indicating heightened cognitive function. This was followed 15-minute later by a pronounced decrease in CFFF values reflecting cognitive degradation presumably as IGN begins taking effect. Surprisingly this impairment persisted upon surfacing and 30-minutes post dive.

This persistence suggests that the old advice of simply ascending a few meters upon experiencing narcosis seems to be an ineffective coping strategy, and would not likely impact CFFF scores. Also surprising was

the initial increase in CFFF values upon reaching depth indicating increased mental arousal. Note that each of the measurements was statistically significant compared to the pre-dive baseline (100%).

According to researchers, these observations are consistent with the <u>proteinic theory</u> of narcosis, which has gained favor in recent times as the dominant mechanism over the older <u>Meyer-Overton theory</u> of anesthesia based on lipid solubility, though both mechanisms are likely in effect. Indeed, it is believed that IGN and anesthesia share the same mechanisms.

The authors hypothesize that the observed effect of brain arousal and associated CFFF values followed by degradation are result of a balance between the direct "drug" effects of nitrogen and oxygen on the GABA receptors and the pharmacokinetics of these interactions. Oxygen exhibits activating effects (in the relevant range of PO_2) on the synthesis, release and recapture of neurotransmitters such as glutamate, dopamine and gamma-aminobutyric acid (GABA), while nitrogen exhibits inhibitory effects, as recently proposed in different studies (See <u>Rostain et al.</u> 2011; <u>Balestra et al</u>. 2018). The next study comparing IGN when breathing air versus enriched air nitrox explores this interaction of oxygen and nitrogen more deeply.

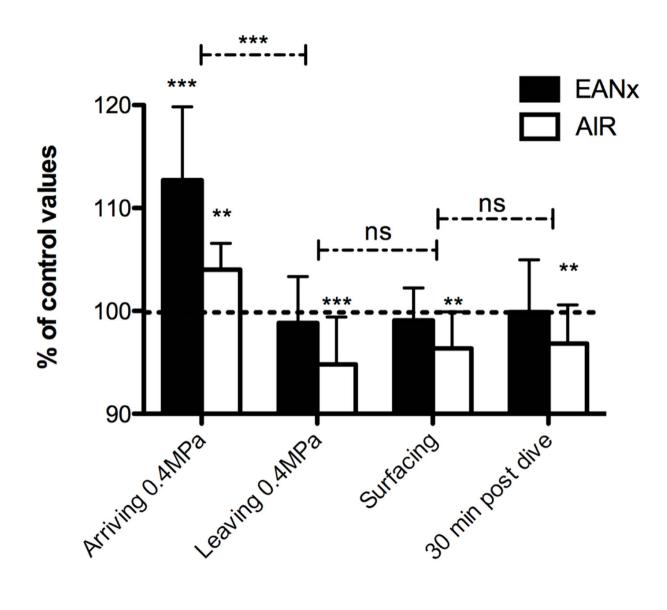
The authors concluded that when objectively measured, that pressure and gas may be the only external factors influencing IGN. <u>However, because the study was not controlled for exertion (i.e. elevated PCO₂s),</u> this could also be, and likely is, a critical factor.

Comparing IGN While Breathing Air Versus EANx

There have been few comparable studies of the effects of breathing air and enriched air nitrox (EAN) on IGN. Some studies have reported worse psychomotor performance when using O2 or EANx, while others have reported that narcotic impairment is the same, though divers may perceive otherwise. The goals of the study were to better understand cognitive performance with differing oxygen partial pressures and the effectiveness of CFFF as a measurement tool.

For this study, researchers selected eight male divers, again 30-40 years old, BMI 20-25. Test dives were conducted on air or EANx 40 in random order in a dry chamber where inspired gases were delivered via face mask. Divers were not aware of the gas they were breathing. The dive profile was designed to produce narcosis: 30m or 4 ATA with a bottom time of 22 minutes, and a 12-minute linear decompression at 3m/minute with a 3-minute safety stop at 3 m.

Divers' cognitive performance were assessed during the dives using both the CFFF testing device and a computerized PEBL test battery consisting of a math processing, trail making and a perceptual vigilance test. Like the previous study, divers were assessed pre-dive, upon arriving at 4 ATA, leaving 4ATA, upon surfacing, 30-min post dive. Researchers also opted to measure oxygenation in divers' prefrontal cortex with a continuous recording of near-infrared spectroscopy (NIRS) oximeter, as another indicator of brain activation.



As shown in Fig. 2 the evolution of CFFF values for both air and EANx showed a similar pattern to that of the first study. When breathing air, CFFF values increased upon arriving at 4ATA, followed 15 minutes later by a decrease. The impairment persisted when surfacing and 30-minutes post dive. Each of the measurements were statistically different. When breathing EANx, CFFF values increased upon arrival of depth, and then decreased after 15 minutes. However, the decrease was followed a return to baseline. Only the first measurement was statistically distinct from baseline.

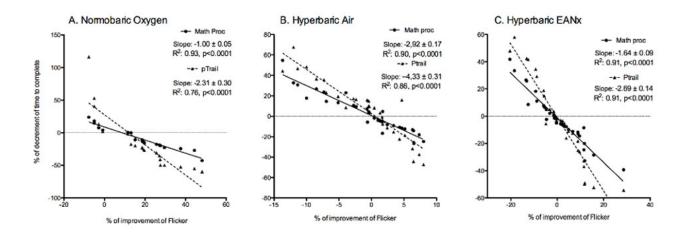


Figure 3 shows the significant inverse correlation between changes in CFFF values and the time required to complete the PEBL math processing and trail-making tasks for both gas mixes. Similar to CFFF values, the time required to complete the PEBL tests decreased i.e. showed improvement upon reaching depth for both gases, and then deteriorated (times were longer) as the dive continued, which persisted 30-minutes post dive. This confirmed the validity of CFFF as a measurement tool for assessing cognitive performance under hyperbaric conditions and suggested that CFFF and PEBL are comparable in their results.

Compressed Air is for Tires?

Though the evolution of the dives showed a similar pattern, there was a significant difference between the two gases. EANx was associated with greater brain activation than found in the air dives, and there was less late dive/post-dive impairment. This was consistent with the NIRS measurements, and the results of the first paper on environmental conditions.

The authors hypothesized the higher fraction of inspired oxygen (PO2=1.6 bar for EAN x 40 vs. 0.8 bar on air) had a beneficial effect on arousal and cognitive performance. This has been shown in other studies on oxygen breathing. This also suggests that divers susceptible to IGN may also be susceptible to the effects of elevated PO₂s. In addition, even a small reduction of PN2 resulted in a <u>beneficial effect of EANx 28</u> (28% oxygen) on cognitive performance in a previous study.

The result? The study gives weight to the meme advanced by Global Underwater Explorers (GUE) that "Compressed Air Is For Tires." Divers are likely to experience less narcosis diving nitrox than air, and nitrox also offers decompression advantages.

Key References

Rocco M, Pelaia P, Di Benedetto P, Conte G, Maggi L, Fiorelli S, Mercieri M, Balestra C, De Blasi RA & Investigators RP. (2019). Inert gas narcosis in scuba diving, different gases different reactions. *Eur J Appl Physiol* 119, 247-255.

Lafere P, Hemelryck W, Germonpre P, Matity L, Guerrero F & Balestra C. (2019). <u>Early detection of diving-</u> related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency. *Diving Hyperb Med* 49, 119-126. Balestra C, Machado ML, Theunissen S, Balestra A, Cialoni D, Clot C, Besnard S, Kammacher L, Delzenne J, Germonpre P & Lafere P. (2018). <u>Critical Flicker Fusion Frequency: A Marker of Cerebral Arousal During</u> <u>Modified Gravitational Conditions Related to Parabolic Flights</u>. *Front Physiol* 9, 1403.

Lafere P, Balestra C, Hemelryck W, Guerrero F & Germonpre P. (2016). <u>Do Environmental Conditions</u> <u>Contribute to Narcosis Onset and Symptom Severity?</u> International journal of sports medicine 37, 1124-1128.

Freiberger JJ, Derrick BJ, Natoli MJ, Akushevich I, Schinazi EA, Parker C, Stolp BW, Bennett PB, Vann RD, Dunworth SA & Moon RE. (2016). <u>Assessment of the interaction of hyperbaric N2, CO2, and O2 on</u> psychomotor performance in divers. *J Appl Physiol (1985)* **121,** 953-964.

Balestra C, Lafere P & Germonpre P. (2012). <u>Persistence of critical flicker fusion frequency impairment</u> <u>after a 33 mfw SCUBA dive: evidence of prolonged nitrogen narcosis?</u> *Eur J Appl Physiol* 112, 4063-4068.

Rostain, J. C., Lavoute, C., Risso, J. J., Vallee, N., and Weiss, M. (2011). <u>A review of recent neurochemical</u> <u>data on inert gas narcosis</u>. *Undersea Hyperb. Med.* 38, 49–59.

Additional Resources:

The Science of Diving: Things your instructor never told you (DAN Member's link - NON Member's link)

About the author

Alert Diver.EU contributing editor Michael Menduno is an award-winning journalist & technologist who has written about diving and diving technology for decades. He coined the term "technical diving." His work has appeared in magazines such as Alert Diver, DeeperBlue.com, DIVER, Quest, Scientific American, Sports Diver, Undercurrent, Undersea Journal, WIRED and X-Ray. He founded and served as editor-in-chief for aquaCORPS Journal (1990-1996), which helped usher tech diving into the mainstream of sports diving. He also produced the first Tek, EuroTek and AsiaTek conferences. In addition, Michael serves as the editor-in-chief of InDepth, Global Underwater Explorers (GUE) online magazine.