EVOLUTION OF VASOVAGAL SYNCOPE: IS THERE A USEFUL PROTECTIVE EFFECT?

JJ BLANC
NO CONFLICT OF INTEREST TO DECLARE
DEFINITION OF VVS

VASOVAGAL (VVS) IS USED TO ENCOMPASS THOSE OCCURRENCES OF SYNCOPE THAT OCCUR IN AN "EMOTIONAL CONTEXT", AND ARE OFTEN REFERRED TO AS THE "COMMON FAINT".
VASOVAGAL SYNCOPE IS COMMON IN HUMANS
CAUSES OF SYNCOPE IN THE EMERGENCY DEPARTMENT

- REFLEX: 49%
- CARDIAC: 36%
- MISCELLANEOUS: 10%
- UNKNOWN: 5%

BLANC EUR HEART J 2002
### EVOLUTION OF CAUSES OF SYNCOPE

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>1980’s</th>
<th>2000’s</th>
<th>2006 *</th>
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<tr>
<td>Neurally-mediated &amp; orthostatic</td>
<td>37%</td>
<td>56%</td>
<td>76%</td>
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<tr>
<td>Cardiac arrhythmias</td>
<td>13%</td>
<td>11%</td>
<td>11%</td>
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<tr>
<td>Structural cardiopulmonary</td>
<td>4%</td>
<td>3%</td>
<td>5%</td>
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<tr>
<td>Non-syncopal</td>
<td>10%</td>
<td>9%</td>
<td>6%</td>
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<tr>
<td>Unexplained</td>
<td>36%</td>
<td>20%</td>
<td>2%</td>
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* Data from EGSYS 2 trial
PROPORTION OF MEDICAL STUDENTS FROM AMSTERDAM WITH SYNCOPE
CONSIDERING THAT PROBABLY ONLY A MINORITY OF THE PATIENTS WITH VVS HAVE A MEDICAL CONSULTATION MORE THAN 50% OF HUMANS EXPERIENCE AT LEAST ONE VVS DURING THEIR LIFETIME.
IS VASO VAGAL SYNCOPE RESTRICTED TO HOMO SAPIENS ?
THERE ARE NO CONVINCING REPORTS ON THE OCCURRENCE OF VASOVAGAL SYNCOPE IN ANIMALS. HOWEVER, SYNCOPE DURING VENIPUNCTURE, A SITUATION THAT COMMONLY LEADS TO SYNCOPE IN HUMANS, HAS PERHAPS BEEN OBSERVED BUT VERY INFREQUENTLY IN CAPTIVE CHIMPANZEEES; BUT "EMOTIONAL" SYNCOPE HAS NOT BEEN DESCRIBED.

VAN DIJK JG. CLIN AUTON RES 2003
IT IS ATTRACTIVE TO CONSIDER THAT VASO VAGAL SYNCOPE IN HUMANS IS AN “ADAPTATION” OF THE “PLAYING DEAD” REACTION IN ANIMALS.
“the opossum reacts with apparent paralysis, prone position, and marked stiffness of the body. Respiratory rate is reduced by about 30%. In some individuals, “playing dead” is accompanied by a decrease in HR (about 50%) as well as the onset of other symptoms of vagal activation, such as salivation, urination, defecation. The animal is conscious, though apparently dead, and at this point the predator loses interest in the potential prey.”

BUT “PLAYING DEAD” IN ANIMALS AND VASO VAGAL SYNCOPE IN HUMANS ARE CLEARLY DIFFERENT ENTITIES

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<tr>
<th></th>
<th>ANIMALS</th>
<th>HUMANS</th>
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</thead>
<tbody>
<tr>
<td>LOOKING DEAD</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>CONSCIOUSNESS</td>
<td>PRESERVED</td>
<td>LOST</td>
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<tr>
<td>PREDOMINENT SYSTEM</td>
<td>SYMPATHETIC</td>
<td>PARASYMPATHETIC</td>
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VASOVAGAL SYNCOPE, VERY FREQUENT IN HOMO SAPIENS, DOES NOT OCCUR IN NON-HUMANS VERTEBRATES.

IT SEEMS THEREFORE THAT VVS IS A REACTION THAT HOMO SAPIENS HAS ACQUIRED DURING EVOLUTION.
WHEN VVS APPEARED?

EVOLUTION OF THE CRANIUM
WHY VVS APPEARED ONLY IN HOMO SAPIENS?
Syncope is a transient loss of consciousness due to transient global cerebral hypo perfusion characterized by rapid onset, short duration, and spontaneous complete recovery.
BECAUSE HUMANS ARE IN UPRIGHT POSITION MOST OF THE TIME (BIPEDALISM)

BRAIN LOCATED IN A CRITICAL SITUATION FOR BLOOD SUPPLY

GRAVITATIONAL STRESS

VERY LARGE CAPACITANCE VASCULAR BED
GRAVITATIONAL SYNCOPE: VVS OCCURS “ALWAYS” IN UPRIGHT OR SITTING POSITION AND “NEVER” LYING DOWN
OVER TIME HUMANS HAVE “LEARNT” TO RESIST TO GRAVITATIONAL FORCES
DIFFERING FROM HUMANS MOST VERTEBRATES HAVE BRAIN AND HEART HORIZONTALLY SITUATED AT ALMOST THE SAME LEVEL

BUT NOT ALL!
GIRAFFE
OSTRICH
BUT THEY DO NOT FAINT !
FINALLY

BIPEDALISM IS CERTAINLY NECESSARY BUT NOT SUFFICIENT TO EXPLAIN WHY VVS IS RESTRICTED TO HUMANS
if “pre humans” had acquired bipedalism for several thousands of years, one would have expected that the species would also have acquired effective adaptive processes to at least limit the very common occurrence of VVS.

LAETOLI TANZANIA (3.7 M YEARS) FOOTPRINTS OF BIPEDS
PARTICULARLY IF WE CONSIDER THE PHYSICAL HARMFUL CONSEQUENCES

494 patients with VVS prospectively included

Bartoletti A et al Eur Heart J 2008
THEREFORE IF VVS HAS PERSISTED IN HUMANS IT CAN BE SPECULATED THAT IT HAS SOME USEFULNESS.
WHAT ARE THE POSSIBLE ADVANTAGES FOR HOMO SAPIENS TO REMAIN A FREQUENT VASO VAGAL FAINTER?
POSSIBLE ADVANTAGES

HEART THEORY

The sudden decrease in SNS and predominance of PNS could protect the heart from the adverse effects of excessive sympathetic drive. This theory has at least 2 major limitations: suppression of SNS activity could be less intense thus avoiding the TLOC and more important:

“careful newer research has documented extensive *Homo sapiens* intragroup warfare in the middle paleolithic. A recurrent cause of death among paleolithic humans was wounding by a sharp object penetrating the skin.”

BRACHA HS et al CNS SPECTRUMS 2004; 9: 679
“PALEOLITHIC” THEORY

“It is unlikely that most non-combatants (females and prepubertal children) could outrun a young male adversary. Hence, the few non-combatants who inherited the polymorphism for fainting response to the first sight of a sharp object or blood now possess a survival advantage.”

In a non-combatant, a genetic polymorphism to abruptly increase vagal tone and collapse flaccidly to the ground rather than flee or fight, could have been selected.”

According to this theory VVS could be consider as a surrogate of the “playing dead strategy” observed in animals.
POSSIBLE ADVANTAGES

“PALEOLITHIC” THEORY

IF THIS THEORY COULD EXPLAIN THE OCCURRENCE OF VVS IN YOUNG INDIVIDUALS AND PARTICULARLY FEMALES IT HAS STRONG LIMITATIONS:

WHY A HAZARDOUS TLOC IS NECESSARY FOR HUMANS TO ESCAPE FROM PREDATORS THROUGH VVS WHILE IN ANIMALS “PLAYING DEAD” FOR THE SAME REASON CONSCIOUSNESS IS FULLY PRESERVED WHICH GIVES THE OPPORTUNITY TO ESCAPE IN A MOMENT OF CARELESSNESS BY THE ASSAILANT?

WHY DID THE EVOLUTION OF VVS WAIT FOR HOMO SAPIENS, SINCE IF IT OFFERS STRONG PROTECTIVE STRATEGY IT COULD HAVE BEEN ADVANTAGEOUS IN OTHER SPECIES (E.G., CHIMPANZEEES) EXPOSED TO AGGRESSION.

POSSIBLE ADVANTAGES

“BLOOD CLOTTING” THEORY

IN THIS CONCEPT, SHUTTING DOWN THE CIRCULATION GIVES MORE CHANCE FOR CLOTTING TO OCCUR AFTER INJURY, AND THEREFORE LIMIT OR EVEN STOP THE HEMORRHAGE.

ANIMALS MAY EXPERIENCE VASOVAGAL REACTIONS RESEMBLING VVS DURING HEMORRHAGE BUT THEY NEED A LOSS OF AROUND 30% OF THEIR TOTAL BLOOD VOLUME TO START “FAINTING”.

THERE ARE NO DATA THAT DEMONSTRATE THAT CIRCULATORY SHUTDOWN PREVENTS DEATH FROM BLEEDING. IN HUMANS, ON THE CONTRARY, IT SEEMS HARMFUL.
POSSIBLE ADVANTAGES

“SUICIDE” THEORY

TO LOSE CONSCIOUSNESS HAS AN EVIDENT CONSEQUENCE: EVENTS HAPPENING DURING THIS PERIOD ARE NO LONGER EXPERIENCED. THEREFORE, AT LEAST IN TERMS OF UNDESIRABLE EXPERIENCES, VVS COULD BE CONSIDERED A MEAN TO ESCAPE TEMPORARILY FROM AN INTOLERABLE WORLD.

IN HUMANS THE PSYCHOLOGICAL BENEFIT OF A TRANSIENT SUICIDE, APPEARS INSUFFICIENT IN THAT IT IS ONLY TRANSITORY AND DOES NOT ADEQUATELY ACCOUNT FOR THE USUAL TRIGGERING SITUATIONS, MOST OF WHICH ARE NOT INTOLERABLE AND SOME EVEN PLEASANT (E.G. INTENSE JOY).
NEWLY CROWNED MISS UNIVERSE FAINTS
FINALLY

THE PRESENT HYPOTHESIS HAVE MAJOR LIMITATIONS AND THEREFORE LOOK AT LEAST PARTIALLY INADEQUATE

WE CLEARLY NEED ANOTHER THEORY
1) Human brain has become disproportionately large and needs a much important proportion of cardiac output compared to other species,
A NEW THEORY

SHOULD INCORPORATE FOUR DEFINITE PIECES OF EVIDENCE

2) VVS provokes a loss of postural tone and a fall,
3) Just before loss of consciousness there is a major “paradoxical” decrease in HR and BP,

![Graph showing HR and BP changes](Image)

A NEW THEORY

SHOULD INCORPORATE FOUR DEFINITE PIECES OF EVIDENCE

3) Just before loss of consciousness there is a major “paradoxical” decrease in HR and BP,
A NEW THEORY

SHOULD INCORPORATE FOUR DEFINITE PIECES OF EVIDENCE

4) Lying down during VVS or returning the table to the horizontal position permits prompt recovery of BP, HR and consciousness.
ONE MAY SPECULATE THAT IF THE HUMAN’S BRAIN SENSES A DECREASE IN BLOOD SUPPLY BELOW A CERTAIN LIMIT, IT INITIATES A SELF-PRESERVATION REFLEX. IN BRIEF, FOLLOWING A PERIOD OF HEIGHTENED ALERTNESS IN WHICH SNS IS FULLY ENGAGED, THE CEREBRUM ACTIVATES THE PNS AND/OR INACTIVATES THE SNS, IN ORDER TO CREATE BRADYCARDIA AND VASODILATATION.

THIS MANEUVER DECREASES BLOOD SUPPLY AND LEADS TO LOSS OF BOTH CONSCIOUSNESS AND POSTURAL TONE; THE FORMER INHERENTLY REDUCES ENERGY CONSUMPTION TEMPORARILY TO BETTER PRESERVE FUNCTIONAL INTEGRITY, WHILE THE LATTER (I.E., THE FALL TO A GRAVITATIONALLY NEUTRAL POSITION) ACTS TO IMPROVE BLOOD SUPPLY DELIVERY TO THE BRAIN BY DIMINISHING THE ADVERSE EFFECT OF GRAVITY.

Blanc JJ, Alboni P, Benditt DG. Europace 2015; 17: 345
SCHEMATIC REPRESENTATION OF CEREBRAL PERFUSION IN A NORMAL SUBJECT AFTER A VASOVAGAL “STRESS” (“EMOTION”)

CHP: Cerebral Hypo Perfusion; CP: Cerebral Perfusion; VVR: Vasovagal reaction
SCHEMATIC REPRESENTATION OF CEREBRAL PERFUSION IN A SUBJECT WITH VVS AFTER A VASOVAGAL “STRESS” (“EMOTION”)

BRAIN “STRUGGLES” THROUGH “NORMAL” ANS ACTIVITY TO KEEP ADEQUATE CP

CRITICAL POINT

“PARADOXICAL” ANS ACTIVITY LEADING TO VVS SUPINE POSITION AND RESTORATION OF CP AND CONSCIOUSNESS

CHP: Cerebral Hypo Perfusion; CP: Cerebral Perfusion; VVR: Vasovagal reaction
CONCLUSION

VVS IS A BEHAVIOUR THAT, AMONG VERTEBRATES, ONLY HOMO SAPIENS EXPERIENCES.

HUMANS’ BRAIN IS DISPROPORTIONALLY LARGE AND IN A CRITICAL SITUATION DUE TO BIPEDALISM.

THIS LARGE CEREBRUM NEEDS A HUGE AND CONSTANT BLOOD FLOW TO WORK (NEURONS HAVE NO ENERGY RESERVE).

TO KEEP THIS CEREBRAL PERFUSION WITHIN THE NORMAL RANGE BRAIN HAS SOPHISTICATED AUTO REGULATION SYSTEMS.

THESE AUTO REGULATION SYSTEMS ARE GENERALLY SUFFICIENT BUT IN CASE OF MAJOR VASOVAGAL REACTIONS (IMPORTANT EMOTIONS, PAIN…) THEY CAN BE OVERFLOWED.

IN THIS SITUATION TO TRY TO IMPROVE THE CEREBRAL PERFUSION LYING DOWN IS THE LAST OPTION (PERFUSION OF THE BRAIN IS FACILITATED IN THE LYING VS UPRIGHT POSITION).
CONCLUSION

TO OBTAIN THIS UNINTENTIONAL AND SOMEWHAT “DANGEROUS” SUPINE POSITION A LOSS OF CONSCIOUSNESSNESS IS NEEDED.

TO OBTAIN TLOC ANS INDUCES BRADYCARDIA/ HYPOTENSION THROUGH A MARKED PNS PREDOMINANCE WHICH, ACCORDING TO THIS INTENTION, LOOKS LOGICAL AND NOT PARADOXICAL.

FINALLY ACCORDING TO THE “BRAIN THEORY” VVS IS “JUST” A NON CONVENTIONNAL AND ULTIMATE PROCESS TO SAVE THE BRAIN FROM HYPOXHEMIA. (IT WORKS AS SUBJECTS WHEN THEY ARE SUPINE RECOVER CONSCIOUSNESSNESS)

FOR HOMO SAPIENS THE BRAIN HAS ACQUIRED SUCH A MAJOR IMPORTANCE THAT IT HAS DEVELOPED ITS OWN SELF PRESERVATION PROCESSES, THE FINAL BEEN VVS, EVEN IF THE PRICE TO PAY FOR THE REST OF THE BODY IS NOT MINOR